10550786

File   5:Biosis Previews(R) 1926-2008/Mar W5
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      Set Items Description
      --- ----- -----------
? s RGD and collagen
           4473 RGD
         121581 COLLAGEN
      S1   537 RGD AND COLLAGEN
? s RGD(2w)enrich?
           4473 RGD
         104870 ENRICH?
      S2   3 RGD(2W)ENRICH?
? t s2/7/1-3

 2/7/1
DIALOG(R)File   5:Biosis Previews(R)

18553925   BIOSIS NO.: 200510248425
Single stage cell seeding of small diameter prosthetic cardiovascular grafts
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AUTHOR ADDRESS: Univ Coll London, Acad Div Surg and Intervent Sci, Biomat and Tissue Engn Ctr, Rowland Hill, London NW3 2PF, UK**UK
AUTHOR E-MAIL ADDRESS: A.Seifalian@MEDSCH.UCL.AC.UK
JOURNAL: Clinical Hemorheology and Microcirculation 33 (3): p209-226 2005 2005
ISSN: 1386-0291
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Small-diameter prosthetic cardiovascular bypass grafts have high occlusion rates. Thrombogenicity caused by the lack of endothelial cells (ECs) on the luminal surface of the grafts is one of the main reasons for its occlusion. One strategy to improve the clinical performance of cardiovascular prosthetic grafts has been to seed its luminal surface with a monolayer of the patient's own ECs. In this strategy a "two stage" seeding procedure is utilized whereby cells obtained from a vein are amplified in cell culture, then seeded onto a fibrin-arginine-glycine-aspartate (%%%RGD%%%) tripeptide-%%%enriched%%% expanded polytetrafluoroethylene (ePTFE) graft in a rotating bioreactor for one week, after which it is surgically implanted. This achieves patency rates approaching those of vein grafts. The disadvantage of two stage seeding is that it requires culture facilities, a large amount of RGD, which is expensive and is confined to elective cases because of the delay between cell cultivation, seeding, and graft implantation. A single stage seeding using freshly extracted ECs that is transplanted onto the graft at the same time frame of the bypass operation without the need for cell cultivation would be an ideal answer for the disadvantages of two stage seeding. Animal trials have been successful but human trials of single stage seeding have been disappointing. It has been hypothesized that extracted ECs are scarce, furthermore, they are washed off the graft

surface once exposed to blood flow. This review examines the various techniques/technologies to improve endothelial cell extraction from various sources and retention onto the luminal surface of prosthetic cardiovascular grafts in order to develop a clinically applicable strategy for single stage seeding.

2/7/2
DIALOG(R)File 5:Biosis Previews(R)

18435477 BIOSIS NO.: 200510129977
Enhanced endothelial cell retention on shear-stressed synthetic vascular grafts precoated with RGD-cross-linked fibrin
AUTHOR: Meinhart Johann G; Schense Jason C; Schima Heinrich; Gorlitzer Michael; Hubbell Jeff A; Deutsch Manfred; Zilla Peter (Reprint)
AUTHOR ADDRESS: Univ Cape Town, Sch Med, Christiaan Barnard Dept Cardiothorac Surg, Cape Heart Ctr, Anzio Rd 2925 Observ, ZA-7925 Cape Town, South Africa**South Africa
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JOURNAL: Tissue Engineering 11 (5-6): p887-895 MAY 05 2005
ISSN: 1076-3279
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Clinical in vitro endothelialization has been shown to increase the patency of synthetic vascular grafts. The shear stress resistance of the cultured autologous endothelium represents a crucial cornerstone of the concept. We investigated whether an enrichment of the precoating matrix with adhesion sites can augment endothelial cell attachment. Adult human saphenous vein endothelial cells (AHSVECs) were seeded confluently ([58 +/- 11] x 10(3) AHSVECs/cm(2)) onto 10-cm-long ePTFE (expanded polytetrafluorethylene) vascular grafts (n = 24) precoated with commercial clinically approved fibrin gel (Tisseal) containing various concentrations of cross- linked RGD peptide (0.0, 4.0, 8.0, or 16.0 mg of RGD per milliliter of Tisseal fibrinogen component). Endothelialized grafts were postcultivated for 9 days before they were exposed to a pulsatile circulation model mimicking peak physiological shear stress conditions of the femoral artery (12 dyn/cm(2); min/max, -60/+28 dyn/cm(2)). Cell loss after 24 h was quantitatively determined by image analysis of vital stains. Initial 24-h cell loss was 27.2 +/- 1.7% in grafts precoated with the non- %%%RGD%%%- %%%enriched%%% fibrin matrix. In contrast, cell loss was significantly less on fibrin containing 4.0 mg of RGD peptide per milliliter of Tisseal fibrinogen component (13.3 +/- 7.9%; $p < 0.05$). Cell loss on fibrin containing 8 and 16 mg of RGD per milliliter of Tisseal fibrinogen component was 41.0 +/- 27.4 and 43.0 +/- 23.2% ($p > 0.05$), respectively. We conclude that low concentrations of RGD peptide cross- linked into commercial fibrin matrices used for clinical in vitro lining of vascular grafts led to significantly increased endothelial cell retention. The failure of higher RGD concentrations to enhance endothelial cell attachment may be explained by competitive binding of endothelial cells to non- cross- linked RGD.

2/7/3
DIALOG(R)File 5:Biosis Previews(R)

13044272 BIOSIS NO.: 199598512105
Convergence of integrin and growth factor receptor signaling pathways within the focal adhesion complex
AUTHOR: Plopper George E; McNamee Helen P; Dike Laura E; Bojanowski Krzysztof; Ingber Donald E (Reprint)
AUTHOR ADDRESS: Enders 1007, Child. Hosp., 300 Longwood Ave., Boston, MA 02115, USA**USA
JOURNAL: Molecular Biology of the Cell 6 (10): p1349-1365 1995 1995
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Extracellular matrix controls capillary endothelial cell sensitivity to soluble mitogens by binding integrin receptors and thereby activating a chemical signaling response that rapidly integrates with growth factor-induced signaling mechanisms. Here we report that in addition to integrins, growth factor receptors and multiple molecules that transduce signals conveyed by both types of receptors are immobilized on the cytoskeleton (CSK) and spatially integrated within the focal adhesion complex (FAC) at the site of integrin binding. FACs were rapidly induced in round cells and physically isolated from the remainder of the CSK after detergent-extraction using magnetic microbeads coated with fibronectin or a synthetic RGD-containing peptide. Immunofluorescence microscopy revealed that multiple signaling molecules (e.g., pp60-c-src, pp125-FAK, phosphatidylinositol-3-kinase, phospholipase C-gamma, and Na+/H+ antiporter) involved in both integrin and growth factor receptor signaling pathways became associated with the CSK framework of the FAC within 15 min after binding to beads coated with integrin ligands. Recruitment of tyrosine kinases to the FAC was also accompanied by a local increase in tyrosine phosphorylation, as indicated by enhanced phosphotyrosine staining at the site of integrin binding. In contrast, neither recruitment of signaling molecules nor increased phosphotyrosine staining was observed when cells bound to beads coated with a control ligand (acetylated low density lipoprotein) that ligates transmembrane scavenger receptors, but does not induce FAC formation. Western blot analysis confirmed that FACs isolated using %%%RGD%%%-beads were %%%enriched%%% for pp60-c-src, pp125-FAK, phospholipase C-gamma, and the Na+/H+ antiporter when compared with intact CSK or basal cell surface preparations that retained lipid bilayer. Isolated FACs were also greatly enriched for the high affinity fibroblast growth factor receptor flg. Most importantly, isolated FACs continued to exhibit multiple chemical signaling activities in vitro, including protein tyrosine kinase activities (pp60-c-src and pp125-FAK) as well as the ability to undergo multiple sequential steps in the inositol lipid synthesis cascade. These data suggest that many of the chemical signaling events that are induced by integrins and growth factor receptors in capillary cells may effectively function in a "solid-state" on insoluble CSK scaffolds within the FAC and that the FAC may represent a major site for signal integration between these two regulatory pathways. Future investigations into the biochemical and biophysical basis of signal transduction may be facilitated by this method, which results in isolation of FACs that retain the CSK framework as well as multiple associated chemical signaling activities.
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Set     Items   Description
S1        537   RGD AND COLLAGEN
S2          3   RGD(2W)ENRICH?
? s s1 and gelatin?
             537  S1
           32869  GELATIN?
      S3      20  S1 AND GELATIN?
? t s3/7/1-20

 3/7/1
DIALOG(R)File   5:Biosis Previews(R)
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0019650159   BIOSIS NO.: 200700309900
Transduction of beta 3 integrin subunit cDNA confers on human keratinocytes
  the ability to adhere to %%%gelatin%%%
AUTHOR: Kubo Miyoko (Reprint); Clark Richard A F; Katz Anne B; Taichman
  Lorne B; Jin Zaishun; Zhao Ying; Moriguchi Takahiko
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JOURNAL: Archives of Dermatological Research  299 (1): p13-24 APR 2007 2007
ISSN: 0340-3696
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: alpha v beta 3 is a multiligand integrin receptor that interacts
  with fibrinogen (FG), fibrin (FB), fibronectin (FN), vitronectin (VN),
  and denatured %%%collagen%%%. We previously reported that cultured normal
  human keratinocytes, like in vivo keratinocytes, do not express alpha v
  beta 3 on the cell surface, and do not adhere to and migrate on FG and
  FB. Furthermore, we reported that human keratinocytes transduced with
  beta 3 integrin subunit cDNA by a retrovirus-mediated transduction method
  express alpha v beta 3 on the cell surface and adhere to FG, FB, FN, and
  VN significantly compared with beta-galactosidase (beta-gal)
  cDNA-transduced keratinocytes (control). In this study, we determined
  whether these beta 3 integrin subunit cDNA-transduced keratinocytes or
  normal human keratinocytes adhere to denatured %%%collagen%%% (
  %%%gelatin%%%) using a 1 h cell adhesion assay. beta 3 cDNA-transduced
  keratinocytes adhered to %%%gelatin%%%, whereas no significant adhesion
  was observed with the control cells (beta-gal cDNA-transduced
  keratinocytes and normal human keratinocytes). The adhesion to
  %%%gelatin%%% was inhibited by LM609, a monoclonal antibody to alpha v
  beta 3, and %%%RGD%%% peptides but not by normal mouse IgG1 nor RGE
  peptides. Thus, transduction of beta 3 integrin subunit cDNA confers on
  human keratinocytes the ability to adhere to denatured %%%collagen%%% (
  %%%gelatin%%%) as well as to FG, FB, VN, and FN. Otherwise, normal human
  keratinocytes do not adhere to %%%gelatin%%%. These data support the idea
  that beta 3 cDNA-transduced human keratinocytes can be a good material
  for cultured epithelium to achieve better take rate with acute or chronic
  wounds, in which FG, FB, and denatured %%%collagen%%% are abundantly
  present.


 3/7/2
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18230486 BIOSIS NO.: 200500137123
Basement membrane proteins play an active role in the invasive process of human hepatocellular carcinoma cells with high metastasis potential
AUTHOR: Tian Bo; Li Yan; Ji Xue-Ning; Chen Jie; Xue Qiong; Ye Sheng-Long; Liu Yin-Kun; Tang Zhao-You (Reprint)
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JOURNAL: Journal of Cancer Research and Clinical Oncology 131 (2): p80-86 February 2005 2005
MEDIUM: print
ISSN: 0171-5216
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Purpose: Cell-matrix adhesive interaction has an important role in the invasive process of tumor cells, and integrins are the major receptors mediating cell-matrix adhesion. The current study is to investigate the modulation of basement membrane (BM) proteins, especially %%%collagen%%% IV (C IV), laminin (LN), and fibronectin (FN) in the invasive processes of human hepatocellular carcinoma (HCC) cells in vitro, and to reveal the roles of beta1 integrins and %%%RGD%%% -containing oligopeptide in the cell-matrix interaction. Methods: Static adhesion assay was performed to study the rates of adhesion of MHCC97-H cells, treated or untreated with anti-beta1 (2 mug ml-1) and GRGDS, to C IV (50 mug ml-1), LN (50 mug ml-1) or FN (50 mug ml-1). %%%Gelatin%%% zymography was used to detect the secretion of MMPs in the conditioned medium of MHCC97-H cells incubated 24 h by C IV, LN or FN, and interactions with anti-beta1 and GRGDS. Transwell chamber assay was used to investigate the influence of C IV, LN or FN, interacting with anti-beta1 and GRGDS, on the cellular mobility of MHCC97-H cells. Results: Compared with blank control group, MHCC97-H cells showed significantly higher rates of adhesion to C IV, LN, and FN. Pretreatment with anti-beta1 could suppress adhesion to C IV, LN or FN, but GRGDS inhibited adhesion to FN ($P < 0.05$) only. LN and FN could stimulate the secretion of MMPs by MHCC97-H cells cultured in vitro, especially MMP-9 and its activated type. Treatment with anti-beta1 could partly counteract the effects of LN and FN. GRGDS could prominently induce the secretion of MMPs, but the effect could be inhibited by pretreatment of anti-beta1. The results of Transwell chamber assay showed that LN, FN, and GRGDS could increase the number of tumor cells penetrating the microporous membrane, but the. data of C IV did not reach significance. The effects were partly counteracted by anti-beta1. Conclusion: BM proteins play an active role in the invasive process of human hepatocellular carcinoma cells. Integrin beta is an important molecule which mediates the cell-matrix adhesive interaction of tumor cells. %%%RGD%%%-containing peptides competitively combine with the binding site of integrin beta1, and the effects of FN are %%%RGD%%% sequence-dependent.

16899507 BIOSIS NO.: 200200493018
An assessment of covalent grafting of %%%RGD%%% peptides to the surface of a compliant poly(carbonate-urea)urethane vascular conduit versus conventional biological coatings: Its role in enhancing cellular retention
AUTHOR: Krijgsman Brandon; Seifalian Alexander M (Reprint); Salacinski Henryk J; Tai Nigel R; Punshon Geoff; Fuller Barry J; Hamilton George
AUTHOR ADDRESS: Biophysics and Tissue Engineering, University Department of Surgery, Royal Free and University College Medical School, The Royal Free Hospital, University College London, Pond Street, London, NW3 2QG, UK**UK
JOURNAL: Tissue Engineering 8 (4): p673-680 August, 2002 2002
MEDIUM: print
ISSN: 1076-3279
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The aim of sodding prosthetic grafts with endothelial cells (EC) is to establish a functioning antithrombogenic monolayer of EC. Application of basement membrane proteins improves EC adherence on ePTFE grafts. Their addition to a biodurable compliant poly(carbonate-urea)urethane graft (CPU) was studied with respect to EC adherence. Preclot, fibronectin, %%%gelatin%%%, and %%%collagen%%% were coated onto CPU. %%%RGD%%% peptide, heparin, and both %%%RGD%%% and heparin were chemically bonded to CPU. Human umbilical vein EC (HUVEC) labeled with 111-Indium oxine were sodded (1.8 X 106 EC/cm2) onto native and the modified CPU. The grafts were washed after 90 min and EC retention determined. The experiments were repeated six times. EC retention on native CPU was 1.0 +- 0.2 X 105 EC/cm2. The application of preclot, fibronectin, %%%gelatin%%%, and %%%collagen%%% did not improve EC retention, which was 0.8 +- 0.1, 0.4 +- 0.1, 0.3 +- 0.08, and 0.5 +- 0.2 X 105 EC/cm2, respectively. Bonding %%%RGD%%%, heparin, and both %%%RGD%%% and heparin significantly improved EC retention to 1.9 +- 0.6, 1.7 +- 0.5, and 2.6 +- 0.6 X 105 EC/cm2, respectively ($p < 0.01$). Bonding of %%%RGD%%%, heparin, and both %%%RGD%%% and heparin accelerates and enhances EC retention onto CPU. Simple coating of basement membrane proteins confers no advantage over native CPU.

3/7/4
DIALOG(R)File 5:Biosis Previews(R)

16868906 BIOSIS NO.: 200200462417
Secreted intestinal surfactant-like particles interact with cell membranes and extracellular matrix proteins in rats
AUTHOR: Mahmood Akhtar; Engle Michael J; Alpers David H (Reprint)
AUTHOR ADDRESS: Department of Medicine, Washington University School of Medicine, 660 S Euclid Ave, Box 8124, St Louis, MO, 63110, USA**USA
JOURNAL: Journal of Physiology (Cambridge) 542 (1): p237-244 1 July, 2002 2002
MEDIUM: print
ISSN: 0022-3751
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Surfactant-like particles (SLP) are secreted from enterocytes basolaterally into the lamina propria, and reach the apical surface through the intercellular tight junctions. Interactions of SLP with apical and basolateral membranes and with extracellular matrix proteins were measured using a solid-phase binding assay and gel overlays. Small-intestinal SLP bound to basolateral membranes much more than to apical membranes, and more tightly to fibronectin than to laminin (affinity constant Ka = 1.23 X 10-2 mug vs. 0.67 X 10-2 mug; maximal number of binding sites 4.1 mug ml-1 vs. 0.32 mug ml-1), but did not bind to %%%collagen%%% types I or IV. Small-intestinal SLP bound fibronectin more than colonic or gastric SLP. Binding to fibronectin was inhibited only partially by %%%RGD%%% peptide and %%%gelatin%%%, but not by heparin. An antibody against alphav integrin also identified the fibronectin-binding component in SLP at apprx220 kDa, which is the expected size for integrin heterodimers. SLP binding to apical microvillous membranes was weaker and was inhibited by heparin. SLP bound more strongly to heparin itself, and this binding was inhibited by glucuronic acid and chondroitin sulfate. These data are consistent with the hypothesis that the time spent by secreted SLP in the lamina propria is prolonged by strong interactions with proteins in the basolateral membranes, and in the intestinal lumen by weaker interactions with apical membrane components, including heparin. These interactions may allow SLP the time to exert their functions in each tissue compartment.

3/7/5

16678258 BIOSIS NO.: 200200271769
Differences in Candida albicans adhesion to intact and denatured type I %%%collagen%%% in vitro
AUTHOR: Makihira S; Nikawa H (Reprint); Tamagami M; Hamada T; Samaranayake L P
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JOURNAL: Oral Microbiology and Immunology 17 (2): p129-131 April, 2002 2002
MEDIUM: print
ISSN: 0902-0055
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An inhibition assay of Candida albicans adhesion to %%%gelatin%%% -immobilized membranes was compared with that to intact type I %%%collagen%%%-immobilized membranes using an arginine-glycine-aspartic acid (%%%RGD%%%) containing peptide. As compared with a protein-free membrane, %%%gelatin%%% and %%%collagen%%% significantly enhanced the adherence of C. albicans. The adhesion of the yeast to %%%gelatin%%% was significantly inhibited by the %%%RGD%%% peptides, but not by arginine-glycine-glutamic acid (RGE) peptides. In contrast, attachment to %%%collagen%%% was not inhibited by %%%RGD%%% peptides. These results suggest that the %%%RGD%%% sequence of %%%gelatin%%% and the integrin-like proteins of yeasts may be involved in adherence.

3/7/6
DIALOG(R)File 5:Biosis Previews(R)

15989361 BIOSIS NO.: 200100161200
Integrins alphavbeta3 and alphavbeta5 mediate VSMC migration and are elevated during neointima formation in the rat aorta
AUTHOR: Kappert Kai; Blaschke Florian; Meehan Woerner P; Kawano Hiroaki; Grill Matthias; Fleck Eckart; Hsueh Willa A; Law Ronald E; Graf Kristof (Reprint)
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JOURNAL: Basic Research in Cardiology 96 (1): p42-49 February, 2001 2001
MEDIUM: print
ISSN: 0300-8428
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neointima formation involves tissue expression of matrix proteins and growth factors. The role of alphavbeta3, but not alphavbeta5 integrin in vascular cells has been sufficiently investigated. The aim of the present study was to determine and compare the function of alphavbeta3 and alphavbeta5 integrins in rat aortic (RASMC) and human coronary vascular smooth muscle cells (HCSMC) and to characterize their expression accompanying neointima formation in vivo. RASMC and HCSMC express alphavbeta3 and alphavbeta5 integrin subunits. The alphavbeta5 integrin predominantly mediated adhesion of RASMCs to vitronectin and spreading on vitronectin via %%%RGD%%%-binding sequences. In contrast, the alphavbeta3 integrin did not contribute to the adhesion and spreading on fibronectin, vitronectin, %%%gelatin%%% or %%%collagen%%% I coated layers. PDGF-directed migration through %%%gelatin%%% coated membranes involved both alphavbeta3 and alphavbeta5 integrins. Selective blocking antibodies for alphavbeta3 and alphavbeta5 inhibited migration of RASMC and HCSMC by more than 60 % ($p < 0.01$). Integrin expression was studied in vivo in thoracic aorta of Sprague Dawley rats before and after balloon injury. In situ hybridization demonstrated low signals for alphav, beta3 and beta5 mRNA in uninjured aorta, which increased significantly at 14 days, localized predominantly in the neointima. Northern analysis of aorta after 14 days of injury also demonstrated an upregulation of alphav, beta3 and beta5 mRNA compared to uninjured aorta. Consistent with the increase in message levels, increased integrin protein expression was seen in the neointima after 7 and 14 days. This study provides evidence that alphavbeta3 and alphavbeta5 are elevated during neointima formation in the rat and indicates a novel role for alphavbeta5 participating in mechanisms regulating smooth muscle cell migration.

3/7/7
DIALOG(R)File 5:Biosis Previews(R)

15877108 BIOSIS NO.: 200100048947
Coordinate induction of collagenase-1, stromelysin-1 and urokinase

plasminogen activator (uPA) by the 120-kDa cell-binding fibronectin fragment in fibrocartilaginous cells: uPA contributes to activation of procollagenase-1
AUTHOR: Hu Bo; Kapila Yvonne L; Buddhikot Madhavee; Shiga Momotoshi; Kapila Sunil (Reprint)
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JOURNAL: Matrix Biology 19 (7): p657-669 December, 2000 2000
MEDIUM: print
ISSN: 0945-053X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Specific fibronectin (Fn) fragments found in synovial fluid of arthritic joints potentially contribute to the loss of cartilage proteoglycans by inducing matrix metalloproteinase (MMP) expression. However, whether or not the Fn fragment-modulated changes in expression of MMPs result in a net increase in matrix-degradative activity through alterations in the balance between MMP activation and inhibition has not been established. To understand the mechanisms by which proteolytic Fn fragments may contribute to joint degeneration, conditioned medium from fibrocartilaginous cells exposed to Fn, its 30-kDa fragment containing the %%%collagen%%%/%%%gelatin%%%-binding domain, its 120-kDa fragment containing the central cell-binding domain, and the %%%RGD%%% peptide were assayed for MMPs, and MMP activators and inhibitors. We found that the 120-kDa fragment of Fn (but not intact Fn), the 30-kDa fragment, and the %%%RGD%%% peptide, dose-dependently induced procollagenase-1 and prostromelysin-1 and decreased levels of the tissue inhibitor of metalloproteinases (TIMPs) -1 and -2. The alpha5beta1 integrin was implicated in the induction of collagenase by the 120-kDa Fn fragment, since collagenase induction was abrogated in the presence of blocking antibody to this integrin. Conditioned medium from cells exposed to the 120-kDa Fn fragment also demonstrated increased levels of the activated collagenase-1, which resulted in significantly elevated %%%collagen%%% degradative activity. That the urokinase plasminogen activator (uPA) was involved in the activation of procollagenase-1 was suggested by findings that the 120-kDa Fn fragment induced uPA coordinately with procollagenase-1, and the activation of procollagenase-1 was dose-dependently inhibited in the presence of plasminogen activator inhibitor-1. These data demonstrate that the 120-kDa cell-binding fragment of Fn induces a net increase in matrix-degradative activity in fibrocartilaginous cells by concomitantly inducing MMPs and their activator, uPA, while decreasing TIMPs.

3/7/8
DIALOG(R)File 5:Biosis Previews(R)

15331925 BIOSIS NO.: 200000050238
Motogenic activity of IGD-containing synthetic peptides
AUTHOR: Schor S L (Reprint); Ellis I; Banyard J; Schor A M
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JOURNAL: Journal of Cell Science 112 (22): p3879-3888 Nov., 1999 1999

MEDIUM: print
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Although the IGD amino acid motif (iso-gly-asp) is a highly conserved feature of the fibronectin type I module, no biological activity has as yet been ascribed to it. We have previously reported that the %%%gelatin%%%-binding domain of fibronectin stimulates the migration of human skin fibroblasts into native, but not denatured, type I %%%collagen%%% substrata. Two IGD-containing type I modules are present within the %%%gelatin%%%-binding domain. The object of this study was to ascertain whether soluble synthetic peptides containing the IGD motif stimulate fibroblast migration. We found that IGD peptides stimulated fibroblast migration in the following order of activity: IGDS (as present in the ninth type I module) > IGDQ (as present in the seventh type I module) > IGD. The scrambled SDGI peptide and the well-characterised RGDS peptide were devoid of motogenic activity. The migratory response of fibroblasts to IGD-containing peptides consisted of two distinct phases: an initial period of peptide-mediated cell activation and a subsequent period of enhanced migration manifest in the absence of further IGD peptide. Cell activation was substratum-independent (occurring equally well on both native and denatured type I %%%collagen%%% substrata), whilst the manifestation of enhanced migration was persistent and substratum-dependent (being evident only by cells adherent to a native %%%collagen%%% substratum). Our data further indicated that cell activation (1) is elicited by a signal transduction cascade occurring within minutes of cell exposure to IGD-containing peptides, (2) is dependent upon integrin alphavbeta3 functionality, (3) involves the tyrosine phosphorylation of focal adhesion kinase (ppFAK125) and (4) is inhibited by signalling mediated through integrin alpha5beta1. The expression of migration stimulating activity by soluble IGD-containing peptides clearly distinguishes them from their %%%RGD%%% counterparts. This is the first identified biological activity of the highly conserved IGD motif and provides a rational platform for the development of a novel family of therapeutic compounds designed to stimulate cell migration in relevant clinical situations, such as impaired wound healing.

3/7/9
DIALOG(R)File 5:Biosis Previews(R)

14592310 BIOSIS NO.: 199800386557
The thrombospondin receptor CD47 (IAP) modulates and associates with alpha2beta1 integrin in vascular smooth muscle cells
AUTHOR: Wang Xue-Qing; Frazier William A (Reprint)
AUTHOR ADDRESS: Box 8231, Dep. Biochem. and Molecular Biophysics, Washington Univ. Sch. Med., 660 S. Euclid Ave., St. Louis, MO 63110, USA **USA
JOURNAL: Molecular Biology of the Cell 9 (4): p865-874 April, 1998 1998
MEDIUM: print
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The carboxyl-terminal domain of thrombospondin-1 enhances the migration and proliferation of smooth muscle cells. Integrin-associated protein (IAP or CD47) is a receptor for the thrombospondin-1 carboxyl-terminal cell-binding domain and binds the agonist peptide 4N1K (kRFYVVMWKk) from this domain. 4N1K peptide stimulates chemotaxis of both human and rat aortic smooth muscle cells on %%%gelatin%%%-coated filters. The migration on %%%gelatin%%% is specifically blocked by monoclonal antibodies against IAP and a beta1 integrin, rather than alphavbeta3 as found previously for 4N1K-stimulated chemotaxis of endothelial cells on %%%gelatin%%%. Both human and rat smooth muscle cells displayed a weak migratory response to soluble type I %%%collagen%%%; however, the presence of 4N1K peptide or intact thrombospondin-1 provoked a synergistic chemotactic response that was partially blocked by antibodies to alpha2 and beta1 integrin subunits and to IAP. A combination of antialpha2 and IAP monoclonal antibodies completely blocked chemotaxis. %%%RGD%%% peptide and antialphavbeta3 mAb were without effect. 4N1K and thrombospondin-1 did not augment the chemotactic response of smooth muscle cells to fibronectin, vitronectin, or collagenase-digested type I %%%collagen%%%. Complex formation between alpha2beta1 and IAP was detected by the coimmunoprecipitation of both alpha2 and beta1 integrin subunits with IAP. These data suggest that IAP can associate with alpha2,beta1 integrin and modulate its function.

13832659 BIOSIS NO.: 199799466719
Characterization of a cartilage-derived 66-kDa protein (%%%RGD%%% -CAP/beta-ig-h3) that binds to %%%collagen%%%
AUTHOR: Hashimoto Kazuto; Noshiro Mitsuhide; Ohno Shigeru; Kawamoto Takeshi ; Satakeda Hisashi; Akagawa Yasumasa; Nakashima Kazuhisa; Okimura Akinobu ; Ishida Hiroko; Okamoto Tetsuji; Pan Haiou; Shen Ming; Yan Weiqun; Kato Yukio (Reprint)
AUTHOR ADDRESS: Dep. Biochem., Sch. Dent., Hiroshima Univ., 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan**Japan
JOURNAL: Biochimica et Biophysica Acta 1355 (3): p303-314 1997 1997
ISSN: 0006-3002
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A 66-kDa %%%collagen%%% fiber-associated protein (%%%RGD%%%-CAP) was isolated from a fiber-rich fraction of pig cartilage by ultrafiltration and %%%collagen%%%-affinity chromatography. Amino acid sequencing and cDNA cloning indicated that the %%%RGD%%%-CAP is identical or closely related to beta-ig-h3 protein which is induced in human adenocarcinoma cells by transforming growth factor-beta (TGF-beta) (Skonier, J., Neubauer, M., Madisen, L., Bennett, K., Plowman, G.D., and Purchio, A.F. (1992) DNA Cell. Biol. II, 511-522). The %%%RGD%%%-CAP, as well as beta-ig-h3, has the %%%RGD%%% sequence in the C-terminal region. The native %%%RGD%%%-CAP bound to type I, II, and IV collagens even in the presence of 1 M NaCl. A recombinant preparation of %%%RGD%%%-CAP expressed in Escherichia coli cells also bound to %%%collagen%%% but not to %%%gelatin%%%. The %%%RGD%%%-CAP mRNA was expressed in chondrocytes

throughout all stages, although the expression level was highest during the prehypertrophic stage. In addition, TGF-beta increased the %%%RGD%%% -CAP mRNA level in chondrocyte cultures. Since %%%RGD%%%-CAP transcripts were found in most tissues, this novel %%%collagen%%%-binding protein may play an important role in cell-%%%collagen%%% interactions in various tissues including developing cartilage.

3/7/11
DIALOG(R)File 5:Biosis Previews(R)

12951560 BIOSIS NO.: 199598419393
Identification of integrins involved in cell adhesion to native and denatured type I collagens and the phenotypic transition of rabbit arterial smooth muscle cells
AUTHOR: Yamamoto Mari; Yamato Masayuki; Aoyagi Masaru; Yamamoto Kiyotaka (Reprint)
AUTHOR ADDRESS: Dep. Cell Biol., Tokyo Metropolitan Inst. Gerontol., 35-2 Sakae-cho, Itabashi-ku, Tokyo 173, Japan**Japan
JOURNAL: Experimental Cell Research 219 (1): p249-256 1995 1995
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Rabbit smooth muscle cells (SMC) in primary culture attached to and started proliferating on native and heat-denatured type I collagens, although the amount of cell attachment to denatured %%%collagen%%% was significantly lower. The cells adhered poorly and were unable to grow on commercial %%%gelatin%%%. In contrast, synthetic SMC in secondary culture could adhere to %%%gelatin%%% and grew as well on %%%gelatin%%% as on native type I %%%collagen%%%. The SMC in the contractile state adhered to native type I %%%collagen%%% through the alpha-1-beta-1 and alpha-3-beta-1 integrins. The cells in the intermediate phenotype also adhered to the substrate through the alpha-1-beta-1 and alpha-3-beta-1 integrins, but the relative amount of a3 integrin decreased. The initial adhesion of cells in secondary culture to native type I %%%collagen%%% was mediated only by the alpha-1-beta-1 integrin. The cell-binding sequences did not contain DGEA (Asp-Gly-Glu-Ala) or %%%RGD%%% (Arg-Gly-Asp). In contrast, cell adhesion to heat-denatured type I %%%collagen%%% was mediated only by the a1-beta-1 integrin in the contractile state and by the alpha-1-beta-1, alpha-2-beta-1, and alpha-3-beta-1 integrins in the synthetic state. In heat-denatured type I %%%collagen%%%, the sequences DGEA and %%%RGD%%% served as a recognition site for the alpha-2-beta-1 and alpha-3-beta-1 integrins. Our results suggest that rabbit SMC can recognize the native and denatured type I collagens through interactions with the triple helix-binding receptors and a chain-binding receptors and that the expression pattern of integrins changes in conjunction with the phenotypic properties of vascular SMC.

3/7/12
DIALOG(R)File 5:Biosis Previews(R)

12178461 BIOSIS NO.: 199497199746
Use of recombinant and synthetic peptides as attachment factors for cells on microcarriers
AUTHOR: Varani James (Reprint); Inman Dennis R; Fligiel Suzanne E G; Hillegas William J
AUTHOR ADDRESS: Dep. Pathol., Univ. Mich. Med. Sch., 1301 Catherine Rd., Box 0602, Ann Arbor, MI 48109, USA**USA
JOURNAL: Cytotechnology 13 (2): p89-98 1993 1993
ISSN: 0920-9069
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Polystyrene culture dishes and polystyrene microcarriers were coated with Pronectin-F and poly-L-lysine (polylysine), either alone or in combination. Pronectin-F is a recombinant peptide containing repeats of the %%%RGD%%% cell-attachment sequence from fibronectin. Polylysine is a polymer of L-lysine. Pronectin-F supported attachment of Madin-Darby Canine Kidney (MDCK) cells at concentrations as low as 0.025 mu-g/cm-2 of surface area. The cells rapidly spread after attachment. Polylysine at concentrations of 0.05-0.5 mu-g/cm-2 also supported cell attachment but cells did not rapidly spread after attachment to this substrate. Higher concentrations of polylysine could not be used because of toxicity. When the two peptides were used in conjunction, MDCK cells attached and spread at lower peptide concentrations than they did when either substrate was used alone. These findings suggest that recombinant Pronectin-F alone or in conjunction with a cationic polymer could be a useful replacement for materials such as %%%gelatin%%% or %%%collagen%%% which are currently used as microcarrier surfaces.

3/7/13
DIALOG(R)File 5:Biosis Previews(R)

11357970 BIOSIS NO.: 199294059811
SPREADING OF HELA CELLS ON A %%%COLLAGEN%%% SUBSTRATUM REQUIRES A SECOND MESSENGER FORMED BY THE LIPOXYGENASE METABOLISM OF ARACHIDONIC ACID RELEASE BY %%%COLLAGEN%%% RECEPTOR CLUSTERING
AUTHOR: CHUN J-S (Reprint); JACOBSON B S
AUTHOR ADDRESS: DEP BIOCHEM AND MOL BIOL, PROGRAM MOL AND CELL BIOL, UNIV MASS, AMHERST, MASS 01003, USA**USA
JOURNAL: Molecular Biology of the Cell 3 (5): p481-492 1992
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: HeLa cells attach to a variety of substrata but spread only on %%%collagen%%% or %%%gelatin%%%. Spreading is dependent on %%%collagen%%% -receptor upregulation, clustering, and binding to the cytoskeleton. This study examines whether second messengers are involved in initiating the spreading process on %%%gelatin%%%. The levels of cytosolic free calcium ([Ca++]i), cAMP, and cytoplasmic pH (pHi) do not change during cell attachment and spreading. However, a basal level of [Ca++]i and an alkaline pHi are required for spreading. There is an activation of protein kinase C (PKC) and a release of arachidonic acid (AA) on

attachment and before cell spreading. Inhibition of PKC does not block cell spreading, indicating that PKC activation is not essential for spreading. Inhibition of phospholipase A2 blocks cell spreading, whereas addition of exogeneous AA overcomes this inhibitory effect. Among AA metabolic pathways, inhibitors of lipoxygenase (LOX) block cell speading, suggesting that a LOX product(s) formed from AA initiates spreading. Clustering receptors for %%%collagen%%% with polyclonal antibodies, or with anti-%%%collagen%%%-receptor antigen-binding fragments (Fab) in combination with a secondary antibody, induce AA release. Also, AA is released when cells attach to either immobilized %%%gelatin%%% or immobilized Arg-Gly-Asp (%%%RGD%%%) peptide. Thus, AA is released whenever receptor clustering is observed. Receptor occupancy is not sufficient to release AA; when cells are treated with %%%gelatin%%% or %%%RGD%%% peptide in solution or anti-%%%collagen%%%-receptor Fab fragments without secondary antibody, conditions where receptor clustering is not observed, AA is not released. Thus, a LOX metabolite(s) of AA formed by %%%collagen%%%-receptor clusering is a second messenger(s) that initiates HeLa cell spreading. LOX inhibitors also block the spreading of bovine aortic endothelial cells, chicken embryo fibroblasts, and CV-1 fibroblasts on %%%gelatin%%% or fibronectin, indicating that other cells might use the same second messenger system in initiating cell-substratum adhesion.

10850306 BIOSIS NO.: 199192096077
RECRUITMENT OF PERIPHERAL MONONUCLEAR CELLS BY MAMMALIAN COLLAGENASE DIGESTS OF TYPE I %%%COLLAGEN%%%
AUTHOR: MALONE J D (Reprint); RICHARDS M; JEFFREY J J
AUTHOR ADDRESS: VAMC, 915 N GRAND, ST LOUIS, MO 63106, USA**USA
JOURNAL: Matrix 11 (4): p289-295 1991
ISSN: 0934-8832
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Type I %%%collagen%%% is highly susceptible to proteolytic cleavage by neutral mamalian collagenase. Following an initial site specific cleavate of the substrate, two characteristic products are generated, TCA and TCB. These two products then spontaneously denature and are degraded into multiple smaller molecular weight peptides. We prepared TCA and TCB from native type I %%%collagen%%% by the action of rat uterine fibroblast neutral collagenase. In addition we prepared denatured type I .alpha. chains and exposed them to the action of collagenase under controlled conditions in order to generate small molecular weight peptides. We then examined intact type I %%%collagen%%%. TCA and TCB and type I %%%gelatin%%% peptides for chemotactic activity in a Boyden chamber assay using both human peripheral monocytes and polymorphonuclear leucocytes as target cells. Intact type I %%%collagen%%%, while chemotactic for neutrophils, failed to elicit any chemotactic response in mononuclear cells. In addition, the results demonstrate an absence of any detectable chemotactic activity for either TCA or TCB when human peripheral monocytes were used as the target cells. However, type I %%%collagen%%% peptides demonstrated chemotactic activity

for peripheral monocytes. Maximum cell migration was found with digests which had been exposed to neutral mammalian collagenase for three to four hours. No chemotractic activity was found using the same peptides, when neutrophils were used as the target cells. The data strongly suggest that chemotactic activity for mononuclear cells, normally suppressed in intact type I %%%collagen%%%, is revealed and/or activated by neutral collagenase digestion. Conversely, chemotactic activity for neutrophils is lost when intact type I %%%collagen%%% is digested into smaller molecular weight fragments. To further examine the mechanism(s) of the directed migratory response to %%%collagen%%% peptides, we used the ubiquitous extracellular matrix tripeptide, ARG-GLY-ASP, present in type I %%%collagen%%%, to probe the chemotactic response to type I %%%gelatin%%% peptides. Arg-Gly-Asp had no intrinsic agonist activity. Co-incubation peripheral mononuclear cells with Arg-Gly-Asp did not block the cell migration response to %%%collagen%%% peptides. These latter observations demonstrate that %%%RGD%%% is not critical for monocyte migration to type I %%%collagen%%% peptides.

10771490 BIOSIS NO.: 199192017261
EFFECTS OF INFLAMMATORY CYTOKINES AND PHORBOL ESTERS ON THE ADHESION OF U937 CELLS A HUMAN MONOCYTE-LIKE CELL LINE TO ENDOTHELIAL CELL MONOLAYERS AND EXTRACELLULAR MATRIX PROTEINS
AUTHOR: CAVENDER D E (Reprint); EDELBAUM D; WELKOVICH L
AUTHOR ADDRESS: DEP MICROBIOL IMMUNOL, UNIV MIAMI SCH MED, PO BOX 016960, MIAMI, FLA 33101, USA**USA
JOURNAL: Journal of Leukocyte Biology 49 (6): p566-578 1991
ISSN: 0741-5400
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The acumulation of mononuclear phagocytes at sites of chronic inflammation is dependent on an increase in the rate of extravasation of blood-borne monocytes through the vascular endothelium into the connective tissue. Once the monocytes have emigrated into the connective tissue, they may differentiate into tissue macrophages, presumably following interactions with extracellular matrix proteins. To study these processes, we tested the effects of cytokines and phorbol esters on the adhesion of U937 cells, a human monocyte-like cell line, to cultured endothelial cells (EC) and to matrix proteins. In the absence of cytokines, very few of the U937 cells adhered to EC (5% or less in most experiments). When EC were pretreated for optimal periods of time (4-8 hr) with recombinant interleukin-1 .alpha. (IL-1.alpha.), IL-1.beta., tumor necrosis factor-.alpha. (TNF.alpha.), or lymphotoxin (LT; also known as TNF-.beta.), 35-85% of the U937 cells were able to bind. Interferon-.gamma. (IFN-.gamma.) and interleukin-2 (IL-2) did not stimulate U937-EC binding, even though IFN-.+-. was shown to increase EC adhesiveness for T lymphocytes. Phorbol esters also greatly stimulated U937-EC adhesion but, in this case, the increase was due to an action on the U937 cells. A monoclonal antibody (MAb), 60.3, against the CD11/CD18 family of leukocyte adhesion molecules partially inhibited the adhesion of untreated and phorbol ester-treated U937 cells to noncytokine-treated

EC. However, that Mab had no effect on U937 cell binding to TNF-.alpha.-treated EC. Thus U937 cells use both CD11/CD18-dependent and -independent mechanisms to adhere to EC. In the absence of stimulating agents, only a small proportion of the U937 cells (2-20%) adhered to fibronectin (FN), and almost none bound to either laminin (LN) or gelation (denatured type I %%%collagen%%%). In the presence of phorbol esters, a much larger proportion of the U937 cells adhered to FN, with only slight increases in the proportion of cells which bound to LN or %%%gelatin%%%. Additional adhesion assays performed in the presence of a pentapeptide containing the amino acid sequence arg-gly-asp (%%%RGD%%%), which is part of one of the cell-binding domains of FN, demonstrated that the %%%RGD%%%-containing peptide almost totally blocked the phorbol ester-induced adhesion of U937 cells to FN. In contrast, the peptide had no inhibitory effect on the phorbol ester-induced binding of U937 cells to EC.

3/7/16
DIALOG(R)File 5:Biosis Previews(R)

10667948 BIOSIS NO.: 199191050839
LIPOPOLYSACCHARIDE ENHANCES MONOCYTE ADHERENCE TO MATRIX-BOUND FIBRONECTIN
AUTHOR: ROTH P (Reprint); POLIN R A
AUTHOR ADDRESS: DIV NEONATOLOGY, DEP PEDIATRICS, ALBERT EINSTEIN COLL MED, BRONX, NY 10461, USA**USA
JOURNAL: Clinical Immunology and Immunopathology 57 (3): p363-373 1990
ISSN: 0090-1229
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Fibronectin (Fn), an extracellular matrix glycoprotein with binding sites for %%%collagen%%%, fibrin, heparin, and cell surfaces, is a nonimmune opsonin which up-regulates phagocytic function and facilitates adherence of human monocytes. We have developed a simple assay to study adherence of peripheral blood monocytes to Fn on a %%%gelatin%%% matrix. While cell adherence was enhanced by the presence of Fn in a dose-dependent manner, it was inhibited by peptides containing the Arg-Gly-Asp (%%%RGD%%%) cell attachment sequence or by coating the matrix with antibodies directed against Fn. Preincubation of monocytes for 30 min with Escherichia coli lipopolysaccharide (LPS) at doses of 1-50 .mu.g/ml increased adherence to Fn-%%%gelatin%%% but not %%%gelatin%%% alone, while longer preincubation (24 hr) resulted in similar changes at lower doses (0.01-1.0 .mu.g/ml). Enhanced Fn adherence may be essential for monocyte localization to sites of inflammation.

3/7/17
DIALOG(R)File 5:Biosis Previews(R)

10633608 BIOSIS NO.: 199191016499
PLATELET C1Q RECEPTOR INTERACTIONS WITH %%%COLLAGEN%%% AND C1Q-COATED SURFACES
AUTHOR: PEERSCHKE E I B (Reprint); GHEBREHIWET B
AUTHOR ADDRESS: UNIVERSITY HOSP, L-3, SUNY AT STONY BROOK, STONY BROOK, NY

11794-7300, USA**USA
JOURNAL: Journal of Immunology 145 (9): p2984-2988 1990
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We recently described specific binding sites for C1q on human blood platelets. Structural similarities between the amino-terminal of C1q and %%%collagen%%% have suggested that receptors for both molecules on platelets might be the same. The present study thus compared the interaction of purified C1q receptors (C1qR) and whole platelets with %%%collagen%%%- and C1q-coated polystyrene surfaces. Surfaces coated with BSA or %%%gelatin%%% served as controls. Purified 125I-labeled C1qR recognized both C1q- and %%%collagen%%%-coated surfaces in a divalent, cation-dependent manner. This adhesion was inhibited by polyclonal or monoclonal (II1/D1) anti-C1qR antibodies. Although C1qR adhered preferentially to C1q-coated surfaces, adhesion to bovine and human type I %%%collagen%%%, as well as to human type III and V %%%collagen%%%, was also noted. In parallel studies, 51Cr-labeled platelets bound equally well to %%%collagen%%%- or C1q-coated surfaces, albeit in a magnesium-dependent manner. Partial inhibition of platelet adhesion was observed in the presence of RGDS, despite the inability of RGDS to modify C1qR interaction with C1q or %%%collagen%%%. Moreover, anti C1qR antibodies selectively inhibited platelet adhesion to C1q-coated surfaces, whereas antibodies specific for the GPIa/IIa %%%collagen%%% receptor (6F1) preferentially inhibited platelet %%%collagen%%% interactions. These data support the presence or distinct platelet membrane C1qR, which may cross-react with %%%collagen%%%, and suggest that C1qR are necessary but not sufficient for platelet adhesion to C1q-coated surfaces. Additional divalent cation and/or %%%RGD%%% -sensitive binding sites may participate.

3/7/18
DIALOG(R)File 5:Biosis Previews(R)

10188709 BIOSIS NO.: 199089106600
INHIBITION OF TUMOR-CELL ATTACHMENT TO EXTRACELLULAR MATRIX AS A METHOD FOR PREVENTING TUMOR RECURRENCE IN A SURGICAL WOUND
AUTHOR: WHALEN G F (Reprint); INGBER D E
AUTHOR ADDRESS: DEP SURG, NEW YORK HOSP CORNELL UNIV MED CENT, 525 EAST 68TH ST, NEW YORK, NY 10021, USA**USA
JOURNAL: Annals of Surgery 210 (6): p758-764 1989
ISSN: 0003-4932
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Studies with four different transplantable murine tumors demonstrated that surgical instruments contaminated by contact with a tumor mass could produce tumors in a surgical wound. Eighty-seven per cent of mice with wounds made by invisibly contaminated scissors developed tumors. Irrigation with water did not prevent tumor growth. Before spilled tumor cells can invade and grow into a recurrence in the wound site, they must first attach to underlying extracellular matrix. We

have devised a simple in vitro assay to identify inhibitors of tumor-cell attachment to develop therapeutic compounds that can prevent tumor-cell reimplantation. Various test compounds, including proteases (trypsin and Dispase), known modulators of matrix metabolism (proline analogues, cycloheximide, heparin, cortisone, cortexolone, and heparin-steroid combinations), large molecular weight polymers (agarose, dextran, polyethylene oxide), and synthetic fibronectin peptides were tested for their ability to inhibit mouse melanoma (B16-F10) cell attachment to %%%gelatinized%%% dishes. Most of these compounds had little or no effect on tumor-cell adhesion when cells were plated in serum-containing medium. However we identified three compounds that inhibited tumor-cell attachment in a reversible fashion: (1) a specific inhibitor of %%%collagen%%% deposition (L-azetidine-2-carboxylic acid); (2) a bacterial neutral protease (Dispase); and (3) synthetic fibronectin peptides that contained the arginine-glycine-asparate (%%%RGD%%%) sequence that is responsible for cell binding. Dispause and the %%%RGD%%% -containing peptides also inhibited cell implantation and prevented tumor formation in a surgical wound. We propose that inhibitors of attachment might be used either alone or with other biologic modifiers to prohibit implantation of free tumor cells at the time of surgery and thus, to prevent local tumor recurrence.

10132905 BIOSIS NO.: 199089050796
INHIBITION OF TUMOR-CELL ATTACHMENT TO EXTRACELLULAR MATRIX AS A METHOD FOR PREVENTING TUMOR RECURRENCE IN A SURGICAL WOUND
AUTHOR: WHALEN G F (Reprint); INGBER D E
AUTHOR ADDRESS: DEP SURGERY, NEW YORK HOSPITAL-CORNELL UNIV MED CENTER, 525 EAST 68TH ST, NEW YORK, NY 10021, USA**USA
JOURNAL: Annals of Surgery 210 (6): p758-764 1989
ISSN: 0003-4932
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Studies with four different transplantable murine tumors demonstrated that surgical instruments contaminated by contact with a tumor mass could produce tumors in a surgical wound. Eighty-seven per cent of mice with wounds made by invisibly contaminated scissors developed tumors. Irrigation with water did not prevent tumor growth. Before spilled tumor cells can invade and grow into a recurrence in the wound site, they must first attach to underlying extracellular matrix. We have derived a simple in vitro assay to identify inhibitors of tumor-cell attachment to develop therapeutic compounds that can prevent tumor-cell reimplantation. Various test compounds, including proteases (trypsin and Dispase), known modulators of matrix metabolism (proline analogues, cycloheximide, heparin, cortisone, cortexolone, and heparin-steroid combinations), large molecular weight polymers (agarose, dextran, polyethylene oxide), and synthetic fibronectin petides were tested for their ability to inhibit mouse melanoma (B16-F10) cell attachment to %%%gelatinized%%% dishes. Most of these compounds had little or no effect on tumor-cell adhesion when cells were plated in serum-containing medium. However, we identified three compounds that inhibited tumor-cell

attachment in a reversible fashion: (1) a specific inhibitor of %%%collagen%%% deposition (L-azetidine-2-carboxylic acid); (2) a bacterial neutral protease (Dispae); and (3) synthetic fibronectin peptides that contained the arginine-glycine (%%%RGD%%%) sequence that is responsible for cell binding. Dispase and the %%%RGD%%%-containing peptides also inhibited cell implantation and prevented tumor formation in a surgical wound. We propose that inhibitors of attachment might be used either alone or with other biologic modifiers to prohibit implantation of free tumor cells at the time of surgery and thus, to prevent local tumor recurrence.

3/7/20
DIALOG(R)File 5:Biosis Previews(R)

09570018 BIOSIS NO.: 198987017909
A %%%COLLAGEN%%%-BINDING PROTEIN INVOLVED IN THE DIFFERENTIATION OF MYOBLASTS RECOGNIZES THE ARG-GLY-ASP SEQUENCE
AUTHOR: NANDAN D (Reprint); CATES G A; BALL E H; SANWAL B D
AUTHOR ADDRESS: DEP BIOCHEM, FAC MED AND DENTISTRY, UNIV WESTERN ONTARIO, LONDON N6A 5C1, CAN**CANADA
JOURNAL: Experimental Cell Research 179 (1): p289-297 1988
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We had earlier demonstrated that a 46-kDa glycoprotein is involved in the differentiation of rat skeletal myoblasts. We now show that the binding of this glycoprotein to %%%collagen%%% and %%%gelatin%%% is disrupted by Arg-Gly-Asp (%%%RGD%%%) containing peptide but not by Arg-Gly-Glu (RGE). The former peptide also selectively elutes the 46-kDa glycoprotein bound to %%%gelatin%%%-Sepharose. Since all other proteins which bind %%%RGD%%% sequences have been found at the cell surface, we attempted to localize the 46-kDa glycoprotein by means of immunofluorescent staining and radioiodine labeling. Surprisingly, the majority of the protein was found to be localized in the endoplasmic reticulum. Protease treatment of a microsomal fraction revealed that the protein is in the interior of the reticulum. Immunoprecipitation experiments, using a polyclonal antibody against the 46-kDa protein, demonstrated that no closely related proteins exist in myoblasts and also confirmed that the protein was not a fragment of a cell-surface localized protein. These findings suggest that the %%%RGD%%% sequence is also used in protein recognition within the cell.
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S1	537	RGD AND COLLAGEN
S2	3	RGD(2W)ENRICH?
S3	20	S1 AND GELATIN?

? (RGD()2w)in()collagen)
>>>RGD()2W)IN()COLL is not a valid accession number in file 5
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            4473 RGD
        13940090 IN
          121581 COLLAGEN
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 4/7/1
DIALOG(R)File   5:Biosis Previews(R)

18284683   BIOSIS NO.: 200500191748
Recruitment of multiple cell lines by collagen-synthetic copolymer matrices in corneal regeneration
AUTHOR: Li F; Griffith M; Li Z; Tanodekaew S; Sheardown H; Hakim M; Carlsson D J (Reprint)
AUTHOR ADDRESS: Inst Chem Proc and Environm Technol, Natl Res Council Canada, 1200 Montreal Rd, Ottawa, ON, K1A 0R6, Canada**Canada
AUTHOR E-MAIL ADDRESS: dave.carlsson@nrc-cnrc.gc.ca
JOURNAL: Biomaterials 26 (16): p3093-3104 June 2005 2005
MEDIUM: print
ISSN: 0142-9612
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Collagen hydrogel matrices with high optical clarity have been developed from collagen 1, cross-linked with a copolymer based on N-isopropylacrylamide, acrylic acid and acryloxysuccinimide. The controlled reaction of collagen amine groups with this copolymer under neutral pH and aqueous conditions gave robust, optically clear hydrogels and prevented the excessive collagen fibrillogenesis that can lead to collagen opacity. These sterile, non-cytotoxic hydrogels allowed epithelial cell overgrowth and both stromal cell and nerve neurite ingrowth from the host tissue. This regenerative ability appeared to result from the high glucose permeability, nanoporosity and the presence of cell adhesion factors, %%%RGD%%% %%%in%%% %%%collagen%%% and the laminin pentapeptide, YIGSR, grafted onto the copolymer. Under physiological conditions, optical clarity superior to the human cornea and tensile performance adequate for suturing were obtained from some formulations. Copyright 2004 Elsevier Ltd. All rights reserved.

 4/7/2
DIALOG(R)File   5:Biosis Previews(R)

15107446   BIOSIS NO.: 199900367106
The effect of advanced glycation end-product formation upon cell-matrix interactions
AUTHOR: Paul R Gordon (Reprint); Bailey Allen J
AUTHOR ADDRESS: Collagen Research Group, Division of Cellular and Molecular Biology, University of Bristol, Langford, Churchill Building, Bristol, BS40 5DS, UK**UK
JOURNAL: International Journal of Biochemistry and Cell Biology 31 (6): p653-660 June, 1999 1999
MEDIUM: print

ISSN: 1357-2725
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The formation of advanced glycation end-products plays a central role in the progressive deterioration of tissues with age, a process that is accelerated in diabetes. Collagen in addition to providing structure and tensile strength to tissues also provides a dynamic matrix for cells to interact with, and due to its long-lived nature is particularly susceptible to modification with age and disease. We have recently identified methylglyoxal as a key intermediate in this process, reacting predominantly with arginine residues to form imidazolone compounds. We therefore postulated that modification of %%%RGD%%% sequences %%%in%%% %%%collagen%%% with methylglyoxal would interfere with crucial cell-matrix interactions. To investigate this concept we studied the interaction of two cell lines, MG63 and HT1080, with collagen modified to varying degrees with respect to arginine. Adhesion and subsequent spreading of both cell lines was significantly decreased by minimal methylglyoxal modification leading to the conclusion that such modification of collagen severely inhibits cell matrix interactions, most likely via the loss of specific arginine residues involved in integrin mediated cell attachment. This is the first demonstration that methylglyoxal modification of collagen can affect cell-matrix interactions and introduces a possible mechanism by which some of the deleterious changes in tissues with age and disease are occurring.
? s gelatin? and RGD
           32869 GELATIN?
            4473 RGD
      S5   59 GELATIN? AND RGD
? s s5 and increase?
              59 S5
         2567611 INCREASE?
      S6   16 S5 AND INCREASE?
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 6/7/1
DIALOG(R)File   5:Biosis Previews(R)

0019468072   BIOSIS NO.: 200700127813
%%%Increased%%% invasive potential and up-regulation of MMP-2 in MDA-MB-231 breast cancer cells expressing the B3 integrin subunit
AUTHOR: Baum Oliver; Hlushchuk Ruslan; Forster Andrea; Greiner Richard; Clezardin Philipp; Zhao Yingshe; Djonov Valentin; Gruber Guenther (Reprint)
AUTHOR ADDRESS: Kantonsspital, Inst Radiat Oncol, Tellstr, CH-5001 Aarau, Switzerland**Switzerland
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JOURNAL: International Journal of Oncology 30 (2): p325-332 FEB 2007 2007
ISSN: 1019-6439
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Intearins are a family of transmembrane adhesion receptors that might transduce signals from the extracellular matrix into the inside of

cells after ligand binding. In order to investigate whether B3 integrins expressed in tumor cells might mediate such outside-in signaling, human MDA-MB-231 breast cancer cells that were stably transfected with either B3 integrin or mock-transfected were investigated in a matrigel degradation assay and a grafting experiment was performed on the developing chicken chorioallantoic membrane (CAM). After cultivation on matrigel for time periods between one and five days, more matrigel was digested in the wells in which 83 integrin expressing cells were incubated than in wells of mock-transfected cells. Furthermore, extracts of B3 integrin expressing cells contained higher levels of MMP-2 protein as determined by immunoblotting and more MMP-2 associated %%%gelatinase%%% activity as detected by zymography than extracts of mock-transfected cells. Matrigel degradation and %%%gelatinase%%% activity as well as MMP-2 expression were elevated when B3 integrin expressing cells were incubated in the presence of the %%%RGD%%% peptide (mimicking an integrin ligand). After grafting on 10 day-old embryonic chicken CAM for three to five days, 63 integrin expressing cells assembled in spheroids showed higher rates of spreading on the CAM surface and CAM invasion as well as a significant MMP-2 up-regulation compared to mock-transfected cells. The results from the in vivo and in vitro experiments allow the conclusion that the presence of 63 integrin in MDA-MB-231 breast cancer cells induced an %%%increased%%% MMP-2 expression and activity that might contribute to the enhanced invasive potential observed.

6/7/2
DIALOG(R)File 5:Biosis Previews(R)

19364900 BIOSIS NO.: 200700024641
Macrophage matrix metalloproteinase-2/-9 gene and protein expression following adhesion to ECM-derived multifunctional matrices via integrin complexation
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LANGUAGE: English

ABSTRACT: Macrophages are commonly observed at the biomaterial-tissue interface and interact with the extracellular matrix (ECM) mainly by integrin receptors to play a critical role in ECM turnover by secreting matrix metalloprotemases (MMPs). To investigate beta 1 and beta 3 containing integrin-mediated adhesion and subsequent MMP-2/-9 protein and gene expression in human blood-derived monocytes, biofunctional peptides immobilized onto flexible polyethylene glycol (PEG) arms were grafted onto a %%%gelatin%%%-based interpenetrating network (IPN). Adherent monocyte density was dramatically greater in the presence of %%%RGD%%% immobilized onto flexible PEG arms of the %%%gelatin%%%-based IPN. Pretreatment of monocytes with either anti-integrin beta 1 or beta 3 led to a significant decrease in adherent cell density on %%%RGD%%% -PEG-grafted IPNs. MMP-2 and MMP-9 protein and MMP-9 mRNA expression

%%%increased%%% in the presence of IPNs initially, independent of ligand identity. Anti-integrin beta 1 or beta 3 antibody pretreatment of monocytes led to a general decrease in MMP-2/-9 protein expression. These results demonstrate the importance of beta 1 and beta 3 containing integrins in mediating monocyte adhesion onto %%%RGD%%% immobilized onto flexible PEG arms of the IPN. The results also reveal that MMP-2/-9 protein and gene expression is influenced by the presence of %%%gelatin%%% and not the ligands immobilized on the PEG arms of the IPN.

6/7/3
DIALOG(R)File 5:Biosis Previews(R)

19364500 BIOSIS NO.: 200700024241
Endothelial cell attachment to the gamma irradiated small diameter polyurethane vascular grafts
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JOURNAL: Bio-Medical Materials and Engineering 16 (6): p397-404 2006 2006
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DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Previously we have fabricated the small diameter polyurethane (Pellethane 2363-80A, abbreviated PU) vascular grafts that were modified by epoxy-crosslinked %%%gelatin%%% (abbreviated %%%gelatin%%%) and an %%%RGD%%%-containing protein (abbreviated CBD-%%%RGD%%%) to facilitate the endothelial cell (EC) seeding on the surface. In this study, the biocompatibility of such surface after freeze-drying and gamma irradiation was evaluated. The contact angle of the irradiated PU dropped a little and the ESCA spectra revealed oxygen bonding. The %%%increases%%% in the amount of extractables as well as in the molecular weight distribution were observed. The mechanical properties decreased only slightly. The irradiated PU surface showed enhanced EC affinity that persisted after several months of storage. %%%Gelatin%%%, CBD-%%%RGD%%% (used with either %%%gelatin%%% or PU), and PU modified by %%%gelatin%%% and CBD-%%%RGD%%% all demonstrated higher EC affinity after freeze-drying and gamma irradiation (2.5 Mrad). The positive cellular effect remained after storage. Based on these results, freeze-drying followed by gamma irradiation at 2.5 Mrad is a proper way to process and store these vascular grafts.

6/7/4
DIALOG(R)File 5:Biosis Previews(R)

18230486 BIOSIS NO.: 200500137123
Basement membrane proteins play an active role in the invasive process of human hepatocellular carcinoma cells with high metastasis potential
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JOURNAL: Journal of Cancer Research and Clinical Oncology 131 (2): p80-86 February 2005 2005
MEDIUM: print
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Purpose: Cell-matrix adhesive interaction has an important role in the invasive process of tumor cells, and integrins are the major receptors mediating cell-matrix adhesion. The current study is to investigate the modulation of basement membrane (BM) proteins, especially collagen IV (C IV), laminin (LN), and fibronectin (FN) in the invasive processes of human hepatocellular carcinoma (HCC) cells in vitro, and to reveal the roles of beta1 integrins and %%%RGD%%%-containing oligopeptide in the cell-matrix interaction. Methods: Static adhesion assay was performed to study the rates of adhesion of MHCC97-H cells, treated or untreated with anti-beta1 (2 mug ml-1) and GRGDS, to C IV (50 mug ml-1), LN (50 mug ml-1) or FN (50 mug ml-1). %%%Gelatin%%% zymography was used to detect the secretion of MMPs in the conditioned medium of MHCC97-H cells incubated 24 h by C IV, LN or FN, and interactions with anti-beta1 and GRGDS. Transwell chamber assay was used to investigate the influence of C IV, LN or FN, interacting with anti-beta1 and GRGDS, on the cellular mobility of MHCC97-H cells. Results: Compared with blank control group, MHCC97-H cells showed significantly higher rates of adhesion to C IV, LN, and FN. Pretreatment with anti-beta1 could suppress adhesion to C IV, LN or FN, but GRGDS inhibited adhesion to FN ($P < 0.05$) only. LN and FN could stimulate the secretion of MMPs by MHCC97-H cells cultured in vitro, especially MMP-9 and its activated type. Treatment with anti-beta1 could partly counteract the effects of LN and FN. GRGDS could prominently induce the secretion of MMPs, but the effect could be inhibited by pretreatment of anti-beta1. The results of Transwell chamber assay showed that LN, FN, and GRGDS could %%%increase%%% the number of tumor cells penetrating the microporous membrane, but the. data of C IV did not reach significance. The effects were partly counteracted by anti-beta1. Conclusion: BM proteins play an active role in the invasive process of human hepatocellular carcinoma cells. Integrin beta is an important molecule which mediates the cell-matrix adhesive interaction of tumor cells. %%%RGD%%%-containing peptides competitively combine with the binding site of integrin beta1, and the effects of FN are %%%RGD%%% sequence-dependent.

6/7/5
DIALOG(R)File 5:Biosis Previews(R)

17414849 BIOSIS NO.: 200300373568
Matrix metalloproteinase expression in breast cancer.
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JOURNAL: Journal of Surgical Research 110 (2): p383-392 April 2003 2003
MEDIUM: print
ISSN: 0022-4804 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: Matrix metalloproteinases (MMPs) have been implicated as possible mediators of invasion and metastasis in some cancers. Our objective was to investigate which MMPs were constitutively expressed in breast tumor cells versus those that could be up-regulated by a number of agents known to affect MMP expression in other cell systems. Methods: We evaluated expression of MMPs 1-16 in breast tumor cell lines MDA-MB-231, T47D, and MCF-7 using semiquantitative RT-PCR and %%%gelatin%%% zymography. Exposure to 12-O-tetradecanoylphorbal-3-acetate (TPA), concanavalin-A (Con-A), the fibronectin-mimetic peptide GRGDSP (%%%RGD%%%), extracellular matrix (ECM) components, and anti-integrin antibodies was used to test for possible MMP up-regulation. Mitogen-activated protein kinase inhibitors (MAPK-I) were used to evaluate signal transduction pathways and regulation of MMP expression. Results: MMPs 1, 2, 7-11, 13, 14, and 16 were constitutively expressed in some tumor cell lines but not in normal breast epithelial cells. Administration of TPA, Con-A, and %%%RGD%%% %%%increased%%% the expression of MMPs 1, 2, 9, and 10. No MMP up-regulation was seen in MDA-MB-231 or MCF-7 after exposure to ECM components or after exposure to anti-integrin antibodies. MAPK-I had no effect on constitutive MMP expression but reduced or abolished the TPA up-regulation of MMP-9 in MDA-MB-231 and MCF-7. Conclusions: Breast tumor cell lines constitutively express a number of MMPs. Because MMP expression can be up-regulated by Con-A, the fibronectin-mimetic peptide %%%RGD%%%, and TPA while being susceptible to inhibition by MAPK antagonists, MAPK signaling appears to play a role in this expression.

6/7/6
DIALOG(R)File 5:Biosis Previews(R)

17209493 BIOSIS NO.: 200300168212
In vitro gene expression by cationized derivatives of an artificial protein with repeated %%%RGD%%% sequences, Pronectin(R).
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JOURNAL: Journal of Controlled Release 86 (1): p169-182 9 January 2003 2003
MEDIUM: print
ISSN: 0168-3659 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The objective of this study is to investigate the efficiency of a non-viral gene carrier with %%%RGD%%% sequences, Pronectin F+ for gene transfection. The Pronectin F+ was cationized by introducing ethylenediamine (Ed), spermidine (Sd), and spermine (Sm) to the hydroxyl

groups while the corresponding %%%gelatin%%% derivative was prepared similarly because %%%gelatin%%% also has one %%%RGD%%% sequence per molecule. The zeta potential and molecular size of Pronectin F+ and %%%gelatin%%% derivatives were examined before and after polyion complexation with a plasmid DNA of luciferase. When complexed with the plasmid DNA at the Pronectin F+/plasmid DNA mixing ratio of 50, the complex exhibited a zeta potential of about 10 mV, which is similar to that of the %%%gelatin%%% derivative-plasmid DNA complex. Irrespective of the type of Pronectin F+ and %%%gelatin%%% derivatives, their complexation enabled the apparent molecular size of plasmid DNA to reduce to about 200 nm, the size decreasing with the %%%increased%%% derivative/plasmid DNA weight mixing ratio. The rat gastric mucosal (RGM)-1 cells treated with both complexes exhibited significantly stronger luciferase activities than free plasmid DNA although the enhanced extent was significant for the Sm derivative compared with the corresponding Ed and Sd derivatives. Cell attachment was enhanced by the Pronectin F+ derivative to a significant high extent compared with the %%%gelatin%%% derivative. The amount of plasmid DNA internalized into the cells was enhanced by the complexation with every Pronectin F+ derivative compared with the %%%gelatin%%% derivative. For both of Pronectin F+ and %%%gelatin%%% carriers, the buffering capacity of Sm derivatives was higher than that of Ed and Sd derivatives and comparable to that of polyethyleneimine. It is likely that the high efficiency of gene transfection for the Sm derivative is due to the superior buffering effect. We conclude that the Sm derivative of Pronectin F+ is promising as a non-viral vector of gene transfection.

15989361 BIOSIS NO.: 200100161200
Integrins alphavbeta3 and alphavbeta5 mediate VSMC migration and are elevated during neointima formation in the rat aorta
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JOURNAL: Basic Research in Cardiology 96 (1): p42-49 February, 2001 2001
MEDIUM: print
ISSN: 0300-8428
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neointima formation involves tissue expression of matrix proteins and growth factors. The role of alphavbeta3, but not alphavbeta5 integrin in vascular cells has been sufficiently investigated. The aim of the present study was to determine and compare the function of alphavbeta3 and alphavbeta5 integrins in rat aortic (RASMC) and human coronary vascular smooth muscle cells (HCSMC) and to characterize their expression accompanying neointima formation in vivo. RASMC and HCSMC express alphavbeta3 and alphavbeta5 integrin subunits. The alphavbeta5 integrin predominantly mediated adhesion of RASMCs to vitronectin and spreading on

vitronectin via %%%RGD%%%-binding sequences. In contrast, the alphavbeta3 integrin did not contribute to the adhesion and spreading on fibronectin, vitronectin, %%%gelatin%%% or collagen I coated layers. PDGF-directed migration through %%%gelatin%%% coated membranes involved both alphavbeta3 and alphavbeta5 integrins. Selective blocking antibodies for alphavbeta3 and alphavbeta5 inhibited migration of RASMC and HCSMC by more than 60 % ($p < 0.01$). Integrin expression was studied in vivo in thoracic aorta of Sprague Dawley rats before and after balloon injury. In situ hybridization demonstrated low signals for alphav, beta3 and beta5 mRNA in uninjured aorta, which %%%increased%%% significantly at 14 days, localized predominantly in the neointima. Northern analysis of aorta after 14 days of injury also demonstrated an upregulation of alphav, beta3 and beta5 mRNA compared to uninjured aorta. Consistent with the %%%increase%%% in message levels, %%%increased%%% integrin protein expression was seen in the neointima after 7 and 14 days. This study provides evidence that alphavbeta3 and alphavbeta5 are elevated during neointima formation in the rat and indicates a novel role for alphavbeta5 participating in mechanisms regulating smooth muscle cell migration.

6/7/8
DIALOG(R)File 5:Biosis Previews(R)

15877108 BIOSIS NO.: 200100048947
Coordinate induction of collagenase-1, stromelysin-1 and urokinase plasminogen activator (uPA) by the 120-kDa cell-binding fibronectin fragment in fibrocartilaginous cells: uPA contributes to activation of procollagenase-1
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JOURNAL: Matrix Biology 19 (7): p657-669 December, 2000 2000
MEDIUM: print
ISSN: 0945-053X
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Specific fibronectin (Fn) fragments found in synovial fluid of arthritic joints potentially contribute to the loss of cartilage proteoglycans by inducing matrix metalloproteinase (MMP) expression. However, whether or not the Fn fragment-modulated changes in expression of MMPs result in a net %%%increase%%% in matrix-degradative activity through alterations in the balance between MMP activation and inhibition has not been established. To understand the mechanisms by which proteolytic Fn fragments may contribute to joint degeneration, conditioned medium from fibrocartilaginous cells exposed to Fn, its 30-kDa fragment containing the collagen/%%%gelatin%%%-binding domain, its 120-kDa fragment containing the central cell-binding domain, and the %%%RGD%%% peptide were assayed for MMPs, and MMP activators and inhibitors. We found that the 120-kDa fragment of Fn (but not intact Fn), the 30-kDa fragment, and the %%%RGD%%% peptide, dose-dependently induced procollagenase-1 and prostromelysin-1 and decreased levels of the tissue inhibitor of metalloproteinases (TIMPs) -1 and -2. The alpha5beta1

integrin was implicated in the induction of collagenase by the 120-kDa Fn fragment, since collagenase induction was abrogated in the presence of blocking antibody to this integrin. Conditioned medium from cells exposed to the 120-kDa Fn fragment also demonstrated %%%increased%%% levels of the activated collagenase-1, which resulted in significantly elevated collagen degradative activity. That the urokinase plasminogen activator (uPA) was involved in the activation of procollagenase-1 was suggested by findings that the 120-kDa Fn fragment induced uPA coordinately with procollagenase-1, and the activation of procollagenase-1 was dose-dependently inhibited in the presence of plasminogen activator inhibitor-1. These data demonstrate that the 120-kDa cell-binding fragment of Fn induces a net %%%increase%%% in matrix-degradative activity in fibrocartilaginous cells by concomitantly inducing MMPs and their activator, uPA, while decreasing TIMPs.

6/7/9

13832659 BIOSIS NO.: 199799466719

Characterization of a cartilage-derived 66-kDa protein (%%%RGD%%% -CAP/beta-ig-h3) that binds to collagen

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JOURNAL: Biochimica et Biophysica Acta 1355 (3): p303-314 1997 1997
ISSN: 0006-3002
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A 66-kDa collagen fiber-associated protein (%%%RGD%%%-CAP) was isolated from a fiber-rich fraction of pig cartilage by ultrafiltration and collagen-affinity chromatography. Amino acid sequencing and cDNA cloning indicated that the %%%RGD%%%-CAP is identical or closely related to beta-ig-h3 protein which is induced in human adenocarcinoma cells by transforming growth factor-beta (TGF-beta) (Skonier, J., Neubauer, M., Madisen, L., Bennett, K., Plowman, G.D., and Purchio, A.F. (1992) DNA Cell. Biol. II, 511-522). The %%%RGD%%%-CAP, as well as beta-ig-h3, has the %%%RGD%%% sequence in the C-terminal region. The native %%%RGD%%%-CAP bound to type I, II, and IV collagens even in the presence of 1 M NaCl. A recombinant preparation of %%%RGD%%%-CAP expressed in Escherichia coli cells also bound to collagen but not to %%%gelatin%%%. The %%%RGD%%%-CAP mRNA was expressed in chondrocytes throughout all stages, although the expression level was highest during the prehypertrophic stage. In addition, TGF-beta %%%increased%%% the %%%RGD%%%-CAP mRNA level in chondrocyte cultures. Since %%%RGD%%%-CAP transcripts were found in most tissues, this novel collagen-binding protein may play an important role in cell-collagen interactions in various tissues including developing cartilage.

6/7/10

13042739 BIOSIS NO.: 199598510572
Signal transduction through chondrocyte integrin receptors induces matrix metalloproteinase synthesis and synergizes with interleukin-1
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JOURNAL: Arthritis and Rheumatism 38 (9): p1304-1314 1995 1995
ISSN: 0004-3591
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Objective. To study the role of signal transduction via integrin receptors in the production of metalloproteinase by rabbit articular chondrocytes. Methods. Confluent, primary rabbit articular chondrocytes (RAC) were incubated for 72 hours in the presence of interleukin-1 (IL-1), Arg-Gly-Asp (%%%RGD%%%) peptide, or a combination of IL-1 and %%%RGD%%% peptide. Media were analyzed for stromelysin enzymatic activity using a 3H-labeled transferrin substrate, and for stromelysin and collagenase protein by Western analysis. %%%Gelatinase%%% activity was analyzed by %%%gelatin%%% zymography. IL-1 receptor antagonist (IL-1Ra) protein was used to determine the involvement of IL-1 in mediating the effects of %%%RGD%%% peptide, and fluorescence-activated cell sorter analysis (FACS) was used to examine the effect of IL-1 on chondrocyte integrin subunit expression. Results. %%%RGD%%% peptides induced chondrocyte synthesis of stromelysin, collagenase, and 92-kd %%%gelatinase%%% B, and %%%increased%%% synthesis of the constitutively expressed 72-kd %%%gelatinase%%% A. Further studies focusing on stromelysin demonstrated that this up-regulation was concentration dependent and that %%%RGD%%% peptides synergized with IL-1 in inducing stromelysin synthesis. %%%RGD%%%-induced stromelysin production was inhibited by the IL-1Ra in a concentration-dependent manner, indicating that induction by %%%RGD%%% requires binding of IL-1 to its receptor. FACS analysis of RAC showed that IL-1 stimulation %%%increased%%% the expression of beta-1 and alpha-v integrin subunits on the chondrocyte surface. Conclusion. Our data demonstrate that signal transduction through chondrocyte integrin receptors up-regulates metalloproteinase expression and that this is likely mediated through induction of IL-1. They also suggest that the binding of adhesion molecules to their chondrocyte integrin receptors reduces the amount of IL-1 required to induce stromelysin synthesis. Upregulation of chondrocyte integrin expression by IL-1 may play a role in the synergistic effects seen with a combination of IL-1 and %%%RGD%%% peptides. Since elevated levels of both IL-1 and adhesion molecules are present in rheumatoid arthritis and osteoarthritis synovial fluid, our data suggest that this interaction may be important in mediating the cartilage destruction accompanying these diseases.

12892583 BIOSIS NO.: 199598360416
Keratinocyte Growth Factor Stimulation of %%%Gelatinase%%% (Matrix Metalloproteinase-9) and Plasminogen Activator in Histiotypic Epithelial Cell Culture
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JOURNAL: Journal of Investigative Dermatology 104 (6): p989-994 1995 1995
ISSN: 0022-202X
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The purpose of this investigation was to examine the role that keratinocyte growth factor (KGF) plays in the control of matrix-degrading protease activity in epithelial cells. The culture conditions had a significant effect on cellular responses to the growth factor. In histiotypic culture on porous-polycarbonate membranes, porcine periodontal ligament epithelial cells responded to KGF with %%%increased%%% 92-kDa %%%gelatinase%%% (matrix metalloproteinase (MMP)-9) activity. No such response was observed in cells maintained on plastic plates. Epidermal growth factor and platelet-derived growth factor also %%%increased%%% MMP-9 activity in the histiotypic cultures of epithelial cells. Addition of heparin with KGF produced a further %%%increase%%% in MMP-9 activity, with heparin alone having no effect. Precoating of polycarbonate membranes with matrix components showed that fibronectin and an engineered poly-%%%RGD%%% molecule substrate were required for KGF plus heparin to %%%increase%%% MMP-9 activity. Precoating plastic culture plates with the same proteins did not generate the same response. Concomitant with %%%gelatinase%%% activity, KGF also %%%increased%%% urokinase-type plasminogen activator in the epithelial cells. Thus, KGF appears to be an important regulator of protease secretion in epithelial cells.

6/7/12
DIALOG(R)File 5:Biosis Previews(R)

11745142 BIOSIS NO.: 199395047408
Interaction of endothelial cells with a laminin A chain peptide (SIKVAV) in vitro and induction of angiogenic behavior in vivo
AUTHOR: Grant Derrick S (Reprint); Kinsella James L; Fridman Rafael; Auerbach Robert; Piasecki Barbara A; Yamada Yoshihiro; Zain Mona; Kleinman Hynda K
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JOURNAL: Journal of Cellular Physiology 153 (3): p614-625 1992
ISSN: 0021-9541
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Endothelial cells are known to bind to laminin, and two peptides derived from the laminin A (CTFALRGDNP) and B1(CDPGYIGSR) chains block the capillary-like tube formation on a laminin-rich basement membrane matrix, Matrigel. In the present study, we have used various in vitro and

in vivo assays to investigate the angiogenic-biologic effects of a third active site in the laminin A chain, CS-RARKQAASIKVAVSADR (designated PA22-2) on endothelial cells. The SIKVAV-containing peptide was as active as the YIGSR-containing peptide for endothelial cell attachment but was less active than either the %%%RGD%%%-containing peptide or intact laminin. Endothelial cells seeded on this peptide appeared fibroblastic with many extended processes, unlike the normal cobblestone morphology observed on tissue culture plastic. In addition, in contrast to normal tube formation on Matrigel, short irregular structures formed, some of which penetrated the matrix and sprouting was more apparent. Analysis of enothelial cell conditioned media of cells cultured in the presence of this peptide indicated degradation of the Matrigel and zymograms demonstrated active collagenase IV (%%%gelatinase%%%) at 68 and 62 Kd. A murine in vivo angiogenesis assay and the chick yolk sac/choriallantoic membrane assays with the peptide demonstrated %%%increased%%% endothelial cell mobilization, capillary branching, and vessel formation. These data suggest that the -SILVAV-site may play an important role in initiating branching and formation of new capillaries from the parent vessels, a behavior that is observed in vivo in response to tumor growth or in the normal vascular response to injury.

11198208 BIOSIS NO.: 199293041099
FIBRONECTIN DEPENDENT MACROPHAGE FIBRIN BINDING
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JOURNAL: Blood 78 (11): p2900-2907 1991
ISSN: 0006-4971
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RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Plasma fibronectin has been shown to %%%increase%%% the binding of fibrin monomer to macrophages in vitro. In the present study we began characterization of the mechanism underlying this fibronectin activity. Fragments of fibronectin containing the amino terminus enhanced macrophage fibrin binding to the same extent as intact fibronectin on an equimolar basis. However, fibronectin fragments containing the %%%gelatin%%%-binding domain or the cell-binding domain, but lacking the amino terminus, had no effect on fibrin binding. Fibronectin enhanced fibrin binding was not affected by the addition of synthetic peptides containing the %%%RGD%%% adhesion sequence. The ability of fibronectin to augment fibrin binding remained after paraformaldehyde fixation of macrophage monolayers. Fixation did not alter the basal levels of fibrin binding by macrophages. Preincubation of macrophages with exogenous fibronectin did not %%%increase%%% the binding of fibrin. Fibronectin enhanced fibrin binding remained unaltered after the removal of endogenous cell surface fibronectin by capping with F(ab')2 fragments of antibodies to fibronectin. These results suggest that the amino terminus of fibronectin supports the attachment of fibrin to macrophages by an initial fluid-phase interaction that precedes cellular binding and does not require a cellular response.

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DIALOG(R)File 5:Biosis Previews(R)

10884983 BIOSIS NO.: 199192130754
SOLUBLE LAMININ AND ARGININE GLYCINE ASPARTIC ACID CONTAINING PEPTIDES DIFFERENTIALLY REGULATE TYPE IV COLLAGENASE MESSENGER RNA ACTIVATION AND LOCALIZATION IN TESTICULAR CELL CULTURE
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JOURNAL: Biology of Reproduction 45 (3): p387-394 1991
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RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Rat testicular cells in culture produce several metalloproteinases including type IV collagenases (Sang et al. Biol Reprod 1990; 43.946-955, 956-964). We have now investigated the regulation of testicular cell type IV collagenase and other metalloproteinases in vitro. Soluble laminin stimulated Sertoli cell type IV collagenase mRNA levels. However, three peptides corresponding to different domains of the laminin molecule (CSRAKQAASIKVASADR, FALRGDNP, CLQDGDVRV) did not influence type IV collagenase mRNA levels. Zymographic analysis of medium collected from these cultures revealed that neither soluble laminin nor any of the peptides influenced 72-kDa type IV collagenase protein levels. However, peptide FALRGDNP resulted in both, a selective %%%increase%%% in two higher molecular-weight metalloproteinases (83 kDa nad 110 kDa) and in an activation of the 72-kDa rat type IV collagenase. Interleukin-1, phorbol ester, testosterone, and FSH did not affect collagenase activation. Immunocytochemical studies demonstrated that the addition of soluble laminin resulted in a redistribution of type IV collagenase from intracellular vesicles to the cell-substrate region beneath the cells. Peptide FALRGDNP induced a change from a vesicular to peripheral plasma membrane type of staining pattern. Zymography of plasma membrane preparations demonstrated triton-soluble %%%gelatinases%%% of 76 kDa, 83 kDa, and 110 kDa and a triton-insoluble %%%gelatinase%%% of 225 kDa. The results indicate that testicular cell type IV collagenase mRNA levels, enzyme activation, and distribution are influenced by laminin and %%%RGD%%%-containing peptides.

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DIALOG(R)File 5:Biosis Previews(R)

10771490 BIOSIS NO.: 199192017261
EFFECTS OF INFLAMMATORY CYTOKINES AND PHORBOL ESTERS ON THE ADHESION OF U937 CELLS A HUMAN MONOCYTE-LIKE CELL LINE TO ENDOTHELIAL CELL MONOLAYERS AND EXTRACELLULAR MATRIX PROTEINS
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JOURNAL: Journal of Leukocyte Biology 49 (6): p566-578 1991
ISSN: 0741-5400
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The acumulation of mononuclear phagocytes at sites of chronic inflammation is dependent on an %%%increase%%% in the rate of extravasation of blood-borne monocytes through the vascular endothelium into the connective tissue. Once the monocytes have emigrated into the connective tissue, they may differentiate into tissue macrophages, presumably following interactions with extracellular matrix proteins. To study these processes, we tested the effects of cytokines and phorbol esters on the adhesion of U937 cells, a human monocyte-like cell line, to cultured endothelial cells (EC) and to matrix proteins. In the absence of cytokines, very few of the U937 cells adhered to EC (5% or less in most experiments). When EC were pretreated for optimal periods of time (4-8 hr) with recombinant interleukin-1 .alpha. (IL-1.alpha.), IL-1.beta., tumor necrosis factor-.alpha. (TNF.alpha.), or lymphotoxin (LT; also known as TNF-.beta.), 35-85% of the U937 cells were able to bind. Interferon-.gamma. (IFN-.gamma.) and interleukin-2 (IL-2) did not stimulate U937-EC binding, even though IFN-.+-. was shown to %%%increase%%% EC adhesiveness for T lymphocytes. Phorbol esters also greatly stimulated U937-EC adhesion but, in this case, the %%%increase%%% was due to an action on the U937 cells. A monoclonal antibody (MAb), 60.3, against the CD11/CD18 family of leukocyte adhesion molecules partially inhibited the adhesion of untreated and phorbol ester-treated U937 cells to noncytokine-treated EC. However, that Mab had no effect on U937 cell binding to TNF-.alpha.-treated EC. Thus U937 cells use both CD11/CD18-dependent and -independent mechanisms to adhere to EC. In the absence of stimulating agents, only a small proportion of the U937 cells (2-20%) adhered to fibronectin (FN), and almost none bound to either laminin (LN) or gelation (denatured type I collagen). In the presence of phorbol esters, a much larger proportion of the U937 cells adhered to FN, with only slight %%%increases%%% in the proportion of cells which bound to LN or %%%gelatin%%%. Additional adhesion assays performed in the presence of a pentapeptide containing the amino acid sequence arg-gly-asp (%%%RGD%%%), which is part of one of the cell-binding domains of FN, demonstrated that the %%%RGD%%%-containing peptide almost totally blocked the phorbol ester-induced adhesion of U937 cells to FN. In contrast, the peptide had no inhibitory effect on the phorbol ester-induced binding of U937 cells to EC.

10667948 BIOSIS NO.: 199191050839
LIPOPOLYSACCHARIDE ENHANCES MONOCYTE ADHERENCE TO MATRIX-BOUND FIBRONECTIN
AUTHOR: ROTH P (Reprint); POLIN R A
AUTHOR ADDRESS: DIV NEONATOLOGY, DEP PEDIATRICS, ALBERT EINSTEIN COLL MED, BRONX, NY 10461, USA**USA
JOURNAL: Clinical Immunology and Immunopathology 57 (3): p363-373 1990
ISSN: 0090-1229
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Fibronectin (Fn), an extracellular matrix glycoprotein with binding sites for collagen, fibrin, heparin, and cell surfaces, is a nonimmune opsonin which up-regulates phagocytic function and facilitates adherence of human monocytes. We have developed a simple assay to study adherence of peripheral blood monocytes to Fn on a %%%gelatin%%% matrix. While cell adherence was enhanced by the presence of Fn in a dose-dependent manner, it was inhibited by peptides containing the Arg-Gly-Asp (%%%RGD%%%) cell attachment sequence or by coating the matrix with antibodies directed against Fn. Preincubation of monocytes for 30 min with Escherichia coli lipopolysaccharide (LPS) at doses of 1-50 .mu.g/ml %%%increased%%% adherence to Fn-%%%gelatin%%% but not %%%gelatin%%% alone, while longer preincubation (24 hr) resulted in similar changes at lower doses (0.01-1.0 .mu.g/ml). Enhanced Fn adherence may be essential for monocyte localization to sites of inflammation.
? ds

Set	Items	Description
S1	537	RGD AND COLLAGEN
S2	3	RGD(2W)ENRICH?
S3	20	S1 AND GELATIN?
S4	2	(RGD(2W)IN()COLLAGEN)
S5	59	GELATIN? AND RGD
S6	16	S5 AND INCREASE?

```
? s (add(3w)RGD()collagen)
           19727  ADD
            4473  RGD
          121581  COLLAGEN
      S7       0  (ADD(3W)RGD()COLLAGEN)
? s insert()RGD
           14046  INSERT
            4473  RGD
      S8       0  INSERT()RGD
? s insert?()RGD
          135763  INSERT?
            4473  RGD
      S9       4  INSERT?()RGD
? t s9/7/1-4

 9/7/1
DIALOG(R)File   5:Biosis Previews(R)
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19023675   BIOSIS NO.: 200600369070
Insertional mutagenesis at positions 520 and 584 of adeno-associated virus type 2 (AAV2) capsid gene and generation of AAV2 vectors with eliminated heparin binding ability and introduced novel tropism
AUTHOR: Shi Xiangqun (Reprint); Fang Guangguang; Shi Wenfang
AUTHOR ADDRESS: Huazhong Univ Sci and Technol, Dept Immunol, Tongji Med Coll, 13 Hangkong Rd, Wuhan 430030, Hubei, Peoples R China**Peoples R China
AUTHOR E-MAIL ADDRESS: wenfangshi@mailcity.com
JOURNAL: Human Gene Therapy 17 (3): p353-361 MAR 2006 2006
ISSN: 1043-0342
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recombinant adeno-associated virus (AAV) vectors are promising in the context of gene therapy because of their ability to mediate efficient gene transfer and stable gene expression. AAV2 uses heparin sulfate as its primary receptor, which is widely expressed on the various tissues and organs. This limits the application of AAV2 in targeting specific tissues. To make an AAV2 vector with modified tropism, we constructed various AAV2 capsid mutants by %%%inserting%%% %%%RGD%%%-4C peptide at position 520 and/or at position 584. Eight mutants were generated, identified, and characterized. Heparin-binding ability was completely abrogated in five mutants, and partially reduced in three mutants. Solid-phase ELISA and gene transduction assays confirmed that the novel tropism is determined by the introduced RGD epitope, which binds to cellular integrin receptor. Our observations suggest that simultaneous modification at both sites, tentatively involved in heparin binding, results in altered tropism and improved transduction efficiency in vitro.

9/7/2
DIALOG(R)File 5:Biosis Previews(R)

18707623 BIOSIS NO.: 200600053018
Genes associated with adeno-associated virus (AAV2) transduction enhancement in the human trabecular meshwork (HTM)
AUTHOR: Borras T (Reprint); Chisolm S S; Bartlett J S; Eaton A M; Xue W
JOURNAL: IOVS 46 (Suppl. S): p1155 2005 2005
CONFERENCE/MEETING: Annual Meeting of the Association-for-Research-in-Vision-and-Ophthalmology Ft Lauderdale, FL, USA May 01 -05, 2005; 20050501
SPONSOR: Assoc Res Vis & Ophthalmol
ISSN: 0146-0404
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Purpose: AAV2 vectors offer great promise for gene therapy due to their long-term gene expression and low immune response. We have shown that HTM is refractory to AAV2 but transduction can be drastically enhanced by co-infecting AAV+ Adenovirus (Ad) (viral particles 1/0.05). Here we investigate mechanisms of AAV transduction in the HTM using a pseudotyped AAV and microarray analysis. Methods: An AAV packaging plasmid encoding capsid proteins with an %%%inserted%%% %%%RGD%%% peptide was constructed by PCR-based mutagenesis. AAV.GFP viruses were generated by triple transfection of the packaging plasmids with a plasmid carrying theCMV-eGFP cassette and ITRs plus Ad helper plasmid. Our Ads: AdNull (carrying no foreign gene), AdhTIG3 (encoding MYOC) and Ad.LacZ (encoding B-gal) have been described. Primary HTM cells were infected with AAV.GFP, pseudotyped AAV.RGD.GFP (moi 5-10) or co-infected with each of the AAV.GFP+Ad combinations. GFP mRNA and DNA were measured by RQ-PCR and normalized with 18S RNA and genomic DNA respectively. Total RNA was processed and hybridized to Affymetrix U95Av2 GeneChips (n=5) at the UNC core facility. Comparisons of co-infected cells (AAV.GFP(+) AdNull, AAV.GFP(+) AdhTIG3 and AAV.GPF+Ad.LacZ) vs. cells infected with AAV.GFP alone, and that of AAV.GFP alone vs mock-infected cells, were analyzed

using Affymetrix software. Results: While AAV transduction levels (GFP mRNA) increased 25-300X in the AAV+Ad coinfected cells, AAV DNA levels inside HTM cells were the same in all conditions. DNA from AAV.RGD.GFP was 2.5X higher than AAV but, likewise, yielded no GFP transduction. Infectionwith AAV.GFP alone induced cellular expression changes higher than 1.4-fold in just 0.7% of the 12,626 genes while AAV+Ads co-infections induced the same change in 8.8.% (+Ad.LacZ), 7.3% (+AdhTIG3) and 3.9% (+AdNull) of the cellular genes. Among the 25 most upregulated genes in all three enhancement co-infections were, as expected, genes involved in inflammatory and stress responses, such IL-6 and heat shock 70 kDa protein; surprisingly, this list also included the CAR receptor and four TM preferred genes: carbonic anhydrase II, secretogranin II, tenascin and versican. Conclusions: The inability of AAV gene transferto HTM is not due to viral cell entry failure. Adenoviral vectors elicit a considerably higher TM cellular expression response than AAV. Identification of genes associated with AAV transduction enhancement could help circumvent the use of Ads and obtain a long-term, low immunogenic gene delivery to the TM.

9/7/3

12751448 BIOSIS NO.: 199598219281
Structure of a conformationally constrained Arg-Gly-Asp sequence inserted into human lysozyme
AUTHOR: Yamada Takao (Reprint); Song Haiwei; Inaka Koji; Shimada Yoshimi; Kikuchi Masakazu; Matsushima Masaaki
AUTHOR ADDRESS: Protein Eng. Res. Inst., 6-2-3 Furuedai, Suita, Osaka 565, Japan**Japan
JOURNAL: Journal of Biological Chemistry 270 (11): p5687-5690 1995 1995
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: To examine the effect of a conformational constraint introduced into the Arg-Gly-Asp (RGD) sequence on cell adhesion activity, we constructed a mutant protein by inserting an RGD-containing sequence flanked by two Cys residues between Val-74 and Asn-75 of human lysozyme. The CRGDSC-inserted lysozyme was expressed in yeast, purified, and designated as Cys-RGD4. Using baby hamster kidney cells, Cys-RGD4 was shown to possess even higher cell adhesion activity than that of the RGDS-inserted lysozyme, RGD4. The Cys-RGD4 protein was co-crystallized with a lysozyme inhibitor, tri-N-acetylchitotriose, and the three-dimensional structure was determined at 1.6- ANG resolution by x-ray crystallography. In contrast to RGD4, the %%%inserted%%% %%%RGD%%% -containing region of Cys-RGD4 was well defined. The structural analysis revealed that the two inserted Cys residues form a new disulfide bond in Cys-RGD4, as expected, and that the RGD region assumes a type II' beta-turn conformation of Gly-Asp with a hydrogen bond between the C=O of Arg and the H-N of Ser. In addition, it was confirmed that two more hydrogen bonds are present in the RGD region of the Cys-RGD4 lysozyme. These results suggest that the conformation of the RGD-containing region is rigid and stable in the Cys-RGD4 molecule and that the type II' beta-turn structure of RGD is essential for binding to integrins with

high affinity.

9/7/4
DIALOG(R)File 5:Biosis Previews(R)

12519000 BIOSIS NO.: 199497540285
Functional analysis and modeling of a conformationally constrained Arg-Gly-Asp sequence inserted into human lysozyme
AUTHOR: Yamada Takao; Uyeda Atsuko; Kidera Akinori; Kikuchi Masakazu (Reprint)
AUTHOR ADDRESS: Protein Eng. Res. Inst., 6-2-3 Furuedai, Suita, Osaka 565, Japan**Japan
JOURNAL: Biochemistry 33 (39): p11678-11683 1994 1994
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: To examine the effect of a conformational constraint introduced into the Arg-Gly-Asp (RGD) sequence on cell adhesion activity, we have constructed mutant proteins by %%%inserting%%% %%%RGD%%%-containing sequences flanked by two Cys residues between Val74 and Asn75 of human lysozyme. CRGDC-, CRGDSC-, and CGRGDSC-inserted mutant lysozymes were expressed in yeast, purified, and designated as CysRGD3, Cys-RGD4, and Cys-RGD5, respectively. In baby hamster kidney cells, these mutants were shown to possess high cell adhesion activity by interaction with vitronectin receptor (integrin alpha-v-beta-3), and this activity is 2-3-fold higher than that of the RGDS-inserted mutant lysozyme, RGD4. The mutant proteins also inhibited the binding of human fibrinogen to its receptor (integrin alpha-IIb-beta-3) at a lower concentration than the RGD4 protein. Peptide mapping and mass spectrometric analyses showed that the two inserted Cys residues in these mutants are linked to each other without any effects on the mode of the four disulfide bonds present in native human lysozyme. These results suggest that the introduction of a conformational constraint into the RGD region significantly increases the cell adhesion activity. The conformation of the RGD region in Cys-RGD4 was modeled by a Monte Carlo simulation. Most of the sampled conformations were grouped into three classes; the first is characterized by an extended Gly conformation, the second assumes a type II' beta turn, and the third has a salt bridge between Arg and Asp. The probability of occurrence in the simulation, as well as the crystal structure of RGD4, suggests that the most probable conformation of RGD belongs to the first class.
? ds

Set	Items	Description
S1	537	RGD AND COLLAGEN
S2	3	RGD(2W)ENRICH?
S3	20	S1 AND GELATIN?
S4	2	(RGD(2W)IN()COLLAGEN)
S5	59	GELATIN? AND RGD
S6	16	S5 AND INCREASE?
S7	0	(ADD(3W)RGD()COLLAGEN)
S8	0	INSERT()RGD
S9	4	INSERT?()RGD

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            4473  RGD
          121581  COLLAGEN
     S10       0  INSERT AND RGD AND COLLAGEN
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            4473  RGD
           32869  GELATIN?
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              59  S5
              16  S6
     S12      43  S5 NOT S6
? t s12/7/1-43

 12/7/1
DIALOG(R)File   5:Biosis Previews(R)
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0019894211   BIOSIS NO.: 200700553952
Interpenetrating polymer networks containing %%%gelatin%%% modified with
  PEGylated %%%RGD%%% and soluble KGF: Synthesis, characterization, and
  application in in vivo critical dermal wound
AUTHOR: Waldeck Heather; Chung Amy S; Kao Weiyuan John (Reprint)
AUTHOR ADDRESS: Univ Wisconsin, Coll Engn, Dept Biomed Engn, Madison, WI
  53706 USA**USA
AUTHOR E-MAIL ADDRESS: wjkao@pharmacy.wisc.edu
JOURNAL: Journal of Biomedical Materials Research  82A (4): p861-871 SEP 15
2007 2007
ITEM IDENTIFIER: doi:10.1002/jbm.a.31054
ISSN: 1549-3296_(print) 1552-4965_(electronic)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The purpose of this study was to, evaluate the biocompatibility
  and the efficacy in wound healing of a %%%gelatin%%%-based
  interpenetrating polymer network (IPN) containing poly(ethylene glycol)
  (PEG)-ylated %%%RGD%%%-and soluble KGF-1 (%%%RGD%%%-IPN+KGF). IPNs were
  applied to full-thickness wounds on a rat model. Wound healing was
  assessed through histological grading of the host response and percent
  area contraction at 2 days, I week, 2 weeks, and 3 weeks. A control IPN
  containing unmodified %%%gelatin%%% (unmod-IPN) and a conventional
  clinical bandage were applied to similar wounds and also evaluated.
  During the first week of healing, the unmod-IPN and conventional dressing
  wound showed a greater amount of contraction than that of %%%RGD%%%
  -IPN+KGF. However, by 3 weeks the extent of wound contraction was
  comparable between treatments. The %%%RGD%%%-IPN+KGF treated wound
  demonstrated lower macrophage and fibroblast densities at 3 weeks as
  compared to unmod-IPN treated wounds. %%%RGD%%%-IPN+KGF acted as a tissue
  scaffold while preventing the entry of foreign bodies, advantages not
  seen with the conventional dressing. The extent of cellularity and
  extracellular matrix organization was higher for wounds healed with
  %%%RGD%%%-IPN+KGF than those healed with unmod-IPN. These results
  indicate that both soluble and immobilized bioactive factors can be
  incorporated into our IPN platform to enhance the rate and the quality of
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dermal wound healing. (c) 2007 Wiley Periodicals, Inc.

12/7/2
DIALOG(R)File 5:Biosis Previews(R)

0019847684 BIOSIS NO.: 200700507425
Either integrin subunit beta 1 or beta 3 is involved in mediating monocyte adhesion, IL-1 beta protein and mRNA expression in response to surfaces functionalized with fibronectin-derived peptides
AUTHOR: Chung Amy S; Gao Qiang; Kao Weiyuan John (Reprint)
AUTHOR ADDRESS: Univ Wisconsin, Sch Pharm, Madison, WI 53705 USA**USA
AUTHOR E-MAIL ADDRESS: wjkao@pharmacy.wisc.edu
JOURNAL: Journal of Biomaterials Science Polymer Edition 18 (6): p713-729 JUN 2007 2007
ITEM IDENTIFIER: doi:10.1163/156856207781034179
ISSN: 0920-5063
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We synthesized %%%gelatin%%%-based, interpenetrating network (IPN) scaffolds immobilized with fibronectin (FN)-derived peptides to assess monocyte-biomaterial interaction. Human primary monocytes were seeded onto peptide-grafted IPN or tissue-culture polystyrene (TCPS) pre-adsorbed with FN or FN-derived peptides. Monocyte cell density on both TCPS and IPN surfaces was higher in the presence of the arginine-glycine-aspartic acid (%%%RGD%%%) peptide. Pretreatment with anti-integrin beta 1 or beta 3 antibody decreased monocyte density on all ligand-modified TCPS and IPN. Interleukin-1 beta (IL-1 beta) protein levels of cells on modified TCPS decreased over time. IL-1 beta expression of monocytes in the presence of IPNs peaked at 24 h and then decreased through 168 h. Ligand identity did not affect IL-1 beta expression in either TCPS or IPN samples. Pretreatment with anti-integrin beta 1 or beta 3 antibody reduced IL-1 beta levels from both TCPS and IPN samples in a ligand-independent manner, particularly at 24 h. Monocytic IL-1 beta mRNA expression in IPN samples without antibody pretreatment was highest at 2 h and decreased over time. IL-1 beta mRNA expression in cells with anti-integrin beta 1 or beta 3 antibody pretreatment was similar to those without antibody pretreatment, except for methoxygrafted IPN samples. The change in IL-1 beta mRNA expression did not correlate with changes in protein expression. The results indicate that monocyte adhesion was affected by the substrate and the %%%RGD%%% sequence and beta 1 or beta 3 containing integrin receptors. beta 1-or beta 3-containing integrin receptors were also involved in IL-1 beta gene and protein expression in monocytes adhered to %%%gelatin%%%-based biomaterial surfaces.

12/7/3
DIALOG(R)File 5:Biosis Previews(R)

0019650159 BIOSIS NO.: 200700309900
Transduction of beta 3 integrin subunit cDNA confers on human keratinocytes the ability to adhere to %%%gelatin%%%

AUTHOR: Kubo Miyoko (Reprint); Clark Richard A F; Katz Anne B; Taichman Lorne B; Jin Zaishun; Zhao Ying; Moriguchi Takahiko
AUTHOR ADDRESS: Kawasaki Med Univ, 577 Matsushima, Okayama 7010192, Japan** Japan
AUTHOR E-MAIL ADDRESS: mkubo@med.kawasaki-m.ac.jp
JOURNAL: Archives of Dermatological Research 299 (1): p13-24 APR 2007 2007
ISSN: 0340-3696
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: alpha v beta 3 is a multiligand integrin receptor that interacts with fibrinogen (FG), fibrin (FB), fibronectin (FN), vitronectin (VN), and denatured collagen. We previously reported that cultured normal human keratinocytes, like in vivo keratinocytes, do not express alpha v beta 3 on the cell surface, and do not adhere to and migrate on FG and FB. Furthermore, we reported that human keratinocytes transduced with beta 3 integrin subunit cDNA by a retrovirus-mediated transduction method express alpha v beta 3 on the cell surface and adhere to FG, FB, FN, and VN significantly compared with beta-galactosidase (beta-gal) cDNA-transduced keratinocytes (control). In this study, we determined whether these beta 3 integrin subunit cDNA-transduced keratinocytes or normal human keratinocytes adhere to denatured collagen (%%%gelatin%%%) using a 1 h cell adhesion assay. beta 3 cDNA-transduced keratinocytes adhered to %%%gelatin%%%, whereas no significant adhesion was observed with the control cells (beta-gal cDNA-transduced keratinocytes and normal human keratinocytes). The adhesion to %%%gelatin%%% was inhibited by LM609, a monoclonal antibody to alpha v beta 3, and %%%RGD%%% peptides but not by normal mouse IgG1 nor RGE peptides. Thus, transduction of beta 3 integrin subunit cDNA confers on human keratinocytes the ability to adhere to denatured collagen (%%%gelatin%%%) as well as to FG, FB, VN, and FN. Otherwise, normal human keratinocytes do not adhere to %%%gelatin%%%. These data support the idea that beta 3 cDNA-transduced human keratinocytes can be a good material for cultured epithelium to achieve better take rate with acute or chronic wounds, in which FG, FB, and denatured collagen are abundantly present.

12/7/4
DIALOG(R)File 5:Biosis Previews(R)

0019519158 BIOSIS NO.: 200700178899
Monocytic U937 adhesion, tumor necrosis factor-alpha and interleukin-1 beta expression in response to %%%gelatin%%%-based networks grafted with arginine-glycine-aspartic acid and proline-histidine-serine-arginine-asparagine oligopeptides
AUTHOR: Gao Qiang; Chung Amy S; Kao Weiyuan John (Reprint)
AUTHOR ADDRESS: Univ Wisconsin, Sch Pharm, Madison, WI 53705 USA**USA
AUTHOR E-MAIL ADDRESS: wjkao@pharmacy.wisc.edu
JOURNAL: Tissue Engineering 13 (1): p179-185 JAN 2007 2007
ISSN: 1076-3279
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In this study we synthesized %%%gelatin%%%-based,

tissue-engineering, interpenetrating network (IPN) scaffolds immobilized with fibronectin (FN)-derived peptides to assess monocyte-biomaterial interaction. Human promonocytic U937 cells were seeded onto peptide-grafted IPN or tissue-culture polystyrene plate (TCPS) pre-adsorbed with FN or FN-derived peptides. The presence of %%%RGD%%% influenced U937 density on IPN. Interleukin-1 beta (IL-1 beta) messenger ribonucleic acid (mRNA) expression in adherent U937 on treated TCPS was slightly upregulated at 4 h. Tumor necrosis factor alpha (TNF-alpha) and IL-1 beta mRNA expression in adherent U937 on all IPNs was generally downregulated at 4 h. This downregulation of IL-1 beta mRNA apparently varied in IPNs grafted with different ligand and was still present at 24h. TNF-alpha and IL-1 beta proteins released from U937 on treated TCPS were comparable with the control at 24h, but TNF-alpha and IL-1 beta protein expression in U937 on IPNs was lower at 24h than on the TCPS control. The results indicate that the tissue-engineering substrate and the bioactive peptides modulate the initial U937 adhesion and the subsequent inflammatory cytokine gene and protein expression.

12/7/5
DIALOG(R)File 5:Biosis Previews(R)

18556684 BIOSIS NO.: 200510251184
alpha beta-crystallin strongly localizes to the leading edges of the cell membrane in migrating lens primary epithelial cells
AUTHOR: Deng P (Reprint); Maddala R; Rao P V
AUTHOR ADDRESS: Duke Univ, Med Ctr, Durham, NC USA**USA
JOURNAL: IOVS 45 (Suppl. 2): pU121 APR 2004 2004
CONFERENCE/MEETING: Annual Meeting of the Association-for-Research-in-Vision-and-Ophthalmology Ft Lauderdale, FL, USA April 24 -29, 2004; 20040424
SPONSOR: Assoc Res Vis & Ophthalmol
ISSN: 0146-0404
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Purpose:To determine the sub-cellular distribution of alpha B-crystallin in semi-confluent and contact-inhibited confluent lens epithelial cell cultures. Methods: Primary lens epithelial cells isolated from porcine lenses were grown to confluence or semi-confluence on %%%gelatin%%% coated glass coverslips or plastic Petri dishes. Cells grown on glass coverslips were immunolabelled for alpha B-crystallin using polyclonal antibodies against recombinant alpha B crystallin or ser59 phosphospecific alpha B-crystallin, along with appropriate controls, and images were recorded using confocal microscopy. Cells were also double-labeled for alpha B-crystallin and either beta-catenin, vinculin, actin or phosphotyrosine. Levels of alpha B-crystallin (both total and phosphorylated) were determined in porcine lens epithelial cell cytosolic, membrane and nuclear fractions by Western blot analysis. Subcellular distribution of alpha B-crystallinwas evaluated in cells pretreated with inhibitors of P38 MAP kinase, ERK kinase, Src kinase, integrins or tyrosine kinases. Results: alpha B-crystallin staining was confined predominantly to cytosolic and nuclear regions in the confluent cells, where as in semi-confluent cells, intense pattern of staining was noted at the leading edges of the cell membrane, using either alpha

B-crystallin or Ser59 phosphopecific alpha B-crystallin polycolonal antibody. Subcellular fractionation and Western blotting revealed enrichment of alpha B-crystallin(both total and phosphospecific) in membrane fractions from semi-confluent lens cells. Interestingly, treatment of semi-confluent cells with inhibitors of P38 MAP kinae (SB 202190, 5 mu M), integrins (%%%RGD%%% peptide, 5 mu M), or Src kinase (PP2, 20 mu M) caused dramatic reduction in all-crystallin staining at theleading edges of the cell membrane. Furthermore, the strong alpha B-crystallin staining at the leading edges of cell membrane appears to co-localize with beta-catenin, phosphotyrosine, and, to some extent, with cortical actin fibers.Conclusions: These preliminary data reveal a predominant localization of alpha B-crystallin at the leading edges of the cell membrane in a phosphorylation-dependent fashion, in semi-confluent, migrating and proliferating lens epithelial cells. Interestingly, alpha B-crystallin also appears to co-localize with other signaling molecules known to participate in cell migration and proliferation.

12/7/6
DIALOG(R)File 5:Biosis Previews(R)

18435484 BIOSIS NO.: 200510129984
Macrophage adhesion on %%%gelatin%%%-based interpenetrating networks grafted with PEGylated %%%RGD%%%
AUTHOR: Phillips Jeffrey M; Kao Weiyuan John (Reprint)
AUTHOR ADDRESS: Univ Wisconsin, Sch Pharm, 777 Highland Ave, Madison, WI 53705 USA**USA
AUTHOR E-MAIL ADDRESS: wjkao@pharmacy.wisc.edu
JOURNAL: Tissue Engineering 11 (5-6): p964-973 MAY 05 2005
ISSN: 1076-3279
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human blood-derived macrophage adhesion on interpenetrating networks (IPNs) composed of PEGylated %%%RGD%%%-modified %%%gelatin%%% and poly(ethylene glycol) diacrylate was studied. The interaction between biomaterial immobilized with biofunctional peptides such as %%%RGD%%% and macrophages is central in the design of tissue-engineering scaffolds. PEGylated %%%RGD%%%-modified %%%gelatin%%% was synthesized via several steps involving PEG derivations and characterized by high-performance liquid chromatography, mass spectroscopy, gel permeation chromatography, and the trinitrobenzenesulfonic acid method. IPNs containing modified or unmodified %%%gelatin%%% were cultured with human macrophages and monitored at 2, 24, 96, and 168 h. At each time point, IPNs containing %%%gelatin%%% modified with PEGylated %%%RGD%%% showed a comparable adherent macrophage density as tissue culture polystyrene and a significantly higher cell density than other IPN formulations containing unmodified %%%gelatin%%% or %%%gelatin%%% modified with PEGylated triglycine. Although surface- immobilized %%%RGD%%% can serve to mediate the adhesion of different cell types on the biomaterial surface, the interaction of %%%RGD%%% with immune/inflammatory cells such as macrophages should also be considered when assessing the potential host response of tissue- engineering scaffolds.

12/7/7
DIALOG(R)File 5:Biosis Previews(R)

18138409 BIOSIS NO.: 200500045159
On the mode of action of thrombin-induced angiogenesis: thrombin peptide,TP508, mediates effects in endothelial cells via alphavbeta3 integrin
AUTHOR: Tsopanoglou Nikos E; Papaconstantinou Matthew E; Flordellis Christodoulos S; Maragoudakis Michael E (Reprint)
AUTHOR ADDRESS: Sch MedDept Pharmacol, Univ Patras, GR-26110, Patras, Greece**Greece
AUTHOR E-MAIL ADDRESS: maragoud@med.upatras.gr
JOURNAL: Thrombosis and Haemostasis 92 (4): p846-857 October 2004 2004
MEDIUM: print
ISSN: 0340-6245
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In a previous report we have presented evidence that thrombin interacts with alphanubeta3 integrin in endothelial cells at the molecular and cellular level. This interaction was shown to be of functional significance in vitro and in vivo and contributed to activation of angiogenesis by thrombin. In the present study, we have used a synthetic thrombin peptide, TP508, which represents residues 183 to 200 of human thrombin. This peptide lacks the catalytic site of thrombin but contains the thrombin %%%RGD%%% sequence. Immobilized (surface-coated) TP508 peptide, like thrombin, supported alphanubeta3 integrin-dependent endothelial cell attachment and haptotactic migration. These effects were specific (a scrambled TP508 peptide was without effect), and dose-dependent. The %%%RGD%%% sequence was essential since a modified TP508 peptide, which contained RAID sequence instead of RIGID, was inactive. Immobilized TP508 peptide stimulated phosphorylation of mitogen-activated protein kinases and focal adhesion kinase, the signal transduction pathways characteristic for integrin activation. On the other hand,TP508 peptide, when in solution, did not mimic other thrombin-promoted angiogenic effects, such as that of activation %%%gelatinase%%% A, upregulation of expression of vascular endothelial growth factor receptor mRNA or prostacyclin PGI2 release in endothelial cells. On the contrary, soluble TP508 acted as an antagonist for the aforementioned effects of thrombin. TP508 peptide inhibited these thrombin-induced effects through a %%%RGD%%% and alphanubeta3-related mechanism. The antagonism with thrombin or thrombin receptor activating peptide was specific and involved at least in part mitogen-activated protein kinases activation. These results point to the importance of RIGID sequence of thrombin in mediating effects on endothelial cells and angiogenesis.

12/7/8
DIALOG(R)File 5:Biosis Previews(R)

17723583 BIOSIS NO.: 200400092352
The %%%RGD%%% story: A personal account.

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JOURNAL: Matrix Biology 22 (6): p459-465 November 2003 2003
MEDIUM: print
ISSN: 0945-053X _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English

12/7/9
DIALOG(R)File 5:Biosis Previews(R)

17627810 BIOSIS NO.: 200300578487
Effects of fibronectin, VEGF and angiostatin on the expression of MMPs through different signaling pathways in the JEG-3 cells.
AUTHOR: Zhang Jian; Cao Yu-Jing; Li Fu-Yang; Li Jing; Yao Li-Bo; Duan En-Kui (Reprint)
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JOURNAL: American Journal of Reproductive Immunology 50 (4): p273-285 October 2003 2003
MEDIUM: print
ISSN: 1046-7408 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: PROBLEM: The objective of this study was to evaluate the possible signal pathway of fibronectin (FN), vascular endothelial growth factor (VEGF) and angiostatin (AS) on the expression of matrix metalloproteinases (MMPs) in JEG-3 cells. METHODS OF STUDY: JEG-3 cells were cultured and were examined for the effect of FN, VEGF and AS on the expression of MMPs by immunocytochemistry, %%%gelatin%%% zymography, Western blot analysis and reverse transcription-polymerase chain reaction (RT-PCR). RESULTS: We found that up-regulation of the expression of MMPs was induced by FN and VEGF through the focal adhesion kinase (FAK)/mitogen-activated protein kinase (MAPK) and Flt-1/p38SAPK/MAPKAPK2 signaling pathways, respectively. Furthermore, AS down-regulated the expression of MMPs through the integrin alphaVbeta3/FAK signaling pathway independent of the integrin-binding motif Arg-Gly-Asp (%%%RGD%%%). CONCLUSION: These data indicate that the expression of MMPs is regulated by many independent factors (such as FN, VEGF and AS) through different signaling pathways which influence the behavior of trophoblast cells.

12/7/10
DIALOG(R)File 5:Biosis Previews(R)

17375410 BIOSIS NO.: 200300333706
Biomedical material for improving the adhesion and proliferation of cells and a modified artificial vessel

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JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1271 (3): June 17, 2003 2003
MEDIUM: e-file
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A novel biomedical material, which is characterized by coating a genetically engineered CBD-%%%RGD%%% peptide layer on the surface of a biomedical material consisting of PU to improve the attachment of tissue cells, such as fibroblasts, epithelial cells and endothelial cells. A modified artificial vessel is also disclosed, wherein the adherence of endothelial cells is enhanced by coating a genetically engineered CBD-%%%RGD%%% containing peptide layer on the inner surface of the artificial vessels pre-modified by cross-linked %%%gelatin%%%, and the adhering capacity and activation of platelets is reduced.

12/7/11
DIALOG(R)File 5:Biosis Previews(R)

17340588 BIOSIS NO.: 200300298407
Integrin alphavbeta3 binding to human alpha5-laminins facilitates FGF-2- and VEGF-induced proliferation of human ECV304 carcinoma cells.
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JOURNAL: European Journal of Cell Biology 82 (3): p105-117 March 2003 2003
MEDIUM: print
ISSN: 0171-9335
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human ECV304 cells respond reproducibly by tube formation to complex basement membrane matrices. Laminins are major glycoproteins of basement membranes. We therefore studied the ability of ECV304 cells to attach to defined laminin isoforms and to fibronectin, and identified the involved laminin receptors. The cells bound poorly to fibronectin, to some extent to laminin-1, whereas laminin-2/4 and -10/11 were strong adhesive substrates. Antibody perturbation assays showed that adhesion to laminin-1 was mediated by integrin alpha6beta1, and adhesion to laminin-2/4 by cooperative activity of integrins alpha3beta1 and alpha6beta1. Adhesion of ECV 304 cells to laminin-10/11 was mainly mediated by integrins alpha3beta1, with minor involvement of alpha6beta1/4 and alphavbeta3. Solid-phase binding assays confirmed that integrin alphavbeta3 binds human laminin-10/11 and -10, in an %%%RGD%%% -dependent fashion. Although integrin alphavbeta3 played a very minor role in cell adhesion to laminin-10/11, this interaction facilitated growth factor-induced proliferation of ECV304 cells. In response to FGF-2 or VEGF, the cells proliferated better when attached on laminin-10/11

than on laminin-1, -2/4, or %%%gelatin%%%. The proliferation induced by the joint application of laminin-10/11 and either one of the growth factors could be blocked by antibodies against integrin alphavbeta3. Fragments of several other basement membrane components are known to interact with alphavbeta3. The current data show that that integrin alphavbeta3 can bind intact alpha5-containing laminin trimers. Since the laminin alpha5 chain is broadly expressed in adult basement membranes, this interaction could be physiologically important. Our data suggest that this interaction is involved in the regulation of cellular responses to growth factors known to be involved in epithelial and endothelial development.

17269700 BIOSIS NO.: 200300238419
Transglutaminase-mediated %%%gelatin%%% matrices incorporating cell adhesion factors as a biomaterial for tissue engineering.
AUTHOR: Ito Akira; Mase Atsunori; Takizawa Yohei; Shinkai Masashige; Honda Hiroyuki; Hata Ken-Ichiro; Ueda Minoru; Kobayashi Takeshi (Reprint)
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JOURNAL: Journal of Bioscience and Bioengineering 95 (2): p196-199 February 2003 2003
MEDIUM: print
ISSN: 1389-1723
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The goal of this work was to develop a novel biomaterial to be used for either wound dressing or as a scaffold for tissue engineering. The biodegradable hydrogels were prepared through cross-linking of %%%gelatin%%% with transglutaminase (TGase) in an aqueous solution. We found that the concentrations of 5 wt% %%%gelatin%%% and 1 unit/ml TGase were optimum for the proliferation of NIH/3T3 fibroblasts. Then, we investigated whether the cell proliferation was enhanced by incorporation of cell adhesion factors into the %%%gelatin%%% hydrogels. Since vitronectin and fibronectin can bind with %%%gelatin%%% by the action of TGase, we added these cell adhesion proteins into the %%%gelatin%%% hydrogels. The hydrogels incorporating these cell adhesion proteins significantly enhanced cell proliferation compared with the %%%gelatin%%% hydrogels without these proteins ($p<0.05$). Two types of synthetic Arg-Gly-Asp (%%%RGD%%%) peptides, RGDLLQ and RGDLLG, were also added to the %%%gelatin%%% solution where RGDLLQ is a substrate of TGase by virtue of a glutamine (Q) residue with an epsilon-amino group and RGDLLG is not. These two %%%RGD%%% peptides enhanced cell proliferation, but RGDLLQ significantly enhanced the proliferation compared with RGDLLG ($p<0.05$). These results suggest that TGase-mediated incorporation of cell adhesion factors into %%%gelatin%%% matrices enhanced cell proliferation and this novel biomaterial is a potent tool for wound dressing or tissue engineering.

12/7/13
DIALOG(R)File 5:Biosis Previews(R)

17067297 BIOSIS NO.: 200300026016
In situ immobilization of proteins and %%%RGD%%% peptide on polyurethane surfaces via poly(ethylene oxide) coupling polymers for human endothelial cell growth.
AUTHOR: Wang Dong-an (Reprint); Ji Jian; Sun Yong-Hong; Shen Jia-cong; Feng Lin-xian; Elisseeff Jennifer H
AUTHOR ADDRESS: Department of Biomedical Engineering, Johns Hopkins University, 3400 North Charles Street, Clark Hall 101, Baltimore, MD, 21218, USA**USA
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JOURNAL: Biomacromolecules 3 (6): p1286-1295 November-December 2002 2002
MEDIUM: print
ISSN: 1525-7797 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A "CBABC"-type pentablock coupling polymer, mesylMPEO, was designed and synthesized to promote human endothelial cell growth on the surfaces of polyurethane biomaterials. The polymer was composed of a central 4,4'-methylenediphenyl diisocyanate (MDI) coupling unit and poly(ethylene oxide) (PEO) spacer arms with methanesulfonyl (mesyl) end groups pendent on both ends. As the presurface modifying additive (pre-SMA), the mesylMPEO was noncovalently introduced onto the poly(ether urethane) (PEU) surfaces by dip coating, upon which the protein/peptide factors (%%%gelatin%%%, albumin, and arginine-glycine-aspartic acid tripeptide (%%%RGD%%%)) were covalently immobilized in situ by cleavage of the original mesyl end groups. The pre-SMA synthesis and PEU surface modification were characterized using nuclear magnetic resonance spectroscopy (1H NMR), attenuated total reflection infrared spectroscopy (ATR-FTIR), and X-ray photoelectron spectroscopy (XPS). Human umbilical vein endothelial cells (HUVEC) were harvested manually by collagenase digestion and seeded on the modified PEU surfaces. Cell adhesion ratios (CAR) and cell proliferation ratios (CPR) were measured using flow cytometry, and the individual cell viability (ICV) was determined by MTT assay. The cell morphologies were investigated by optical inverted microscopy (OIM) and scanning electrical microscopy (SEM). The %%%gelatin%%%- and %%%RGD%%%-modified surfaces were HUVEC-compatible and promoted HUVEC growth. The albumin-modified surfaces were compatible but inhibited cell adhesion. The results also indicated that, for HUVEC in vitro cultivation, the cell adhesion stage was of particular importance and had a significant impact on the cell responses to the modified surfaces.

12/7/14
DIALOG(R)File 5:Biosis Previews(R)

16899507 BIOSIS NO.: 200200493018
An assessment of covalent grafting of %%%RGD%%% peptides to the surface of a compliant poly(carbonate-urea)urethane vascular conduit versus conventional biological coatings: Its role in enhancing cellular

retention
AUTHOR: Krijgsman Brandon; Seifalian Alexander M (Reprint); Salacinski Henryk J; Tai Nigel R; Punshon Geoff; Fuller Barry J; Hamilton George
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JOURNAL: Tissue Engineering 8 (4): p673-680 August, 2002 2002
MEDIUM: print
ISSN: 1076-3279
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The aim of sodding prosthetic grafts with endothelial cells (EC) is to establish a functioning antithrombogenic monolayer of EC. Application of basement membrane proteins improves EC adherence on ePTFE grafts. Their addition to a biodurable compliant poly(carbonate-urea)urethane graft (CPU) was studied with respect to EC adherence. Preclot, fibronectin, %%%gelatin%%%, and collagen were coated onto CPU. %%%RGD%%% peptide, heparin, and both %%%RGD%%% and heparin were chemically bonded to CPU. Human umbilical vein EC (HUVEC) labeled with 111-Indium oxine were sodded (1.8 X 106 EC/cm2) onto native and the modified CPU. The grafts were washed after 90 min and EC retention determined. The experiments were repeated six times. EC retention on native CPU was 1.0 +- 0.2 X 105 EC/cm2. The application of preclot, fibronectin, %%%gelatin%%%, and collagen did not improve EC retention, which was 0.8 +- 0.1, 0.4 +- 0.1, 0.3 +- 0.08, and 0.5 +- 0.2 X 105 EC/cm2, respectively. Bonding %%%RGD%%%, heparin, and both %%%RGD%%% and heparin significantly improved EC retention to 1.9 +- 0.6, 1.7 +- 0.5, and 2.6 +- 0.6 X 105 EC/cm2, respectively ($p < 0.01$). Bonding of %%%RGD%%%, heparin, and both %%%RGD%%% and heparin accelerates and enhances EC retention onto CPU. Simple coating of basement membrane proteins confers no advantage over native CPU.

12/7/15
DIALOG(R)File 5:Biosis Previews(R)

16868906 BIOSIS NO.: 200200462417
Secreted intestinal surfactant-like particles interact with cell membranes and extracellular matrix proteins in rats
AUTHOR: Mahmood Akhtar; Engle Michael J; Alpers David H (Reprint)
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JOURNAL: Journal of Physiology (Cambridge) 542 (1): p237-244 1 July, 2002 2002
MEDIUM: print
ISSN: 0022-3751
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Surfactant-like particles (SLP) are secreted from enterocytes basolaterally into the lamina propria, and reach the apical surface through the intercellular tight junctions. Interactions of SLP with apical and basolateral membranes and with extracellular matrix proteins

were measured using a solid-phase binding assay and gel overlays. Small-intestinal SLP bound to basolateral membranes much more than to apical membranes, and more tightly to fibronectin than to laminin (affinity constant Ka = 1.23 X 10-2 mug vs. 0.67 X 10-2 mug; maximal number of binding sites 4.1 mug ml-1 vs. 0.32 mug ml-1), but did not bind to collagen types I or IV. Small-intestinal SLP bound fibronectin more than colonic or gastric SLP. Binding to fibronectin was inhibited only partially by %%%RGD%%% peptide and %%%gelatin%%%, but not by heparin. An antibody against alphav integrin also identified the fibronectin-binding component in SLP at apprx220 kDa, which is the expected size for integrin heterodimers. SLP binding to apical microvillous membranes was weaker and was inhibited by heparin. SLP bound more strongly to heparin itself, and this binding was inhibited by glucuronic acid and chondroitin sulfate. These data are consistent with the hypothesis that the time spent by secreted SLP in the lamina propria is prolonged by strong interactions with proteins in the basolateral membranes, and in the intestinal lumen by weaker interactions with apical membrane components, including heparin. These interactions may allow SLP the time to exert their functions in each tissue compartment.

12/7/16
DIALOG(R)File 5:Biosis Previews(R)

16678258 BIOSIS NO.: 200200271769
Differences in Candida albicans adhesion to intact and denatured type I collagen in vitro
AUTHOR: Makihira S; Nikawa H (Reprint); Tamagami M; Hamada T; Samaranayake L P
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JOURNAL: Oral Microbiology and Immunology 17 (2): p129-131 April, 2002 2002
MEDIUM: print
ISSN: 0902-0055
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An inhibition assay of Candida albicans adhesion to %%%gelatin%%% -immobilized membranes was compared with that to intact type I collagen-immobilized membranes using an arginine-glycine-aspartic acid (%%%RGD%%%) containing peptide. As compared with a protein-free membrane, %%%gelatin%%% and collagen significantly enhanced the adherence of C. albicans. The adhesion of the yeast to %%%gelatin%%% was significantly inhibited by the %%%RGD%%% peptides, but not by arginine-glycine-glutamic acid (RGE) peptides. In contrast, attachment to collagen was not inhibited by %%%RGD%%% peptides. These results suggest that the %%%RGD%%% sequence of %%%gelatin%%% and the integrin-like proteins of yeasts may be involved in adherence.

12/7/17
DIALOG(R)File 5:Biosis Previews(R)

16576298 BIOSIS NO.: 200200169809
A new pseudo-peptide of Arg-Gly-Asp (%%%RGD%%%) inhibits intrahepatic metastasis of orthotopically implanted murine hepatocellular carcinoma
AUTHOR: Tsuchiya Yasunori; Sawada Shigeaki; Tsukada Kazuhiro; Saiki Ikuo (Reprint)
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JOURNAL: International Journal of Oncology 20 (2): p319-324 February, 2002 2002
MEDIUM: print
ISSN: 1019-6439
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have previously reported that the expression of matrix metalloproteinase-9 (MMP-9), membrane type-1 matrix metalloproteinase (MT1-MMP) and beta1 integrins in murine hepatocellular carcinoma (HCC) was associated with the occurrence of intrahepatic metastasis, which is considered to be a major modality in recurrence. Here we show that intravenous administration of synthetic %%%RGD%%% pseudo-peptide (FC-336) inhibited intrahepatic metastasis produced by orthotopic implantation of a fragment of murine HCC (CBO140C12) tumor as compared with control administration of vehicle ($p<0.05$), but did not affect the growth of the implanted tumor. To further analyze the anti-metastatic effect of FC-336, we investigated the effects of FC-336 on tumor growth, adhesion and invasion in vitro. FC-336 at non-cytotoxic concentration of less than 5 mg/ml effectively inhibited the adhesion and invasion of CBO140C12 cells ($p<0.05$). We also used zymography to examine the effect of FC-336 on the %%%gelatinolysis%%% of MMPs produced by CBO140C12 cells. FC-336 inhibited the degradation of the %%%gelatin%%% substrate by MMP-9 in a concentration-dependent manner. These results strongly suggest that intrahepatic metastasis of CBO140C12 tumors is partly due to the marked invasive and adhesive abilities of tumor cells mediated by expression of MMP-9 and integrin alpha3beta1 (VLA-3), integrin alpha5beta1 (VLA-5) on the tumor surface, respectively.

12/7/18
DIALOG(R)File 5:Biosis Previews(R)

16571889 BIOSIS NO.: 200200165400
Salmosin, a novel disintegrin from the Korean snake venom, suppresses the proliferation of human melanoma cells on %%%gelatin%%% by inducing apoptosis via blocking integrin alpha(v)
AUTHOR: Kang In-Cheol (Reprint); Kim Sung-Hoon (Reprint); Han Kyu-Yeon (Reprint); Chung Kwang-Hoe; Kim Doo-Sik
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JOURNAL: Molecular Biology of the Cell 12 (Supplement): p321a Nov, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 41st Annual Meeting of the American Society for Cell

Biology Washington DC, USA December 08-12, 2001; 20011208
SPONSOR: American Society for Cell Biology
ISSN: 1059-1524
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

15331925 BIOSIS NO.: 200000050238
Motogenic activity of IGD-containing synthetic peptides
AUTHOR: Schor S L (Reprint); Ellis I; Banyard J; Schor A M
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JOURNAL: Journal of Cell Science 112 (22): p3879-3888 Nov., 1999 1999
MEDIUM: print
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Although the IGD amino acid motif (iso-gly-asp) is a highly conserved feature of the fibronectin type I module, no biological activity has as yet been ascribed to it. We have previously reported that the %%%gelatin%%%-binding domain of fibronectin stimulates the migration of human skin fibroblasts into native, but not denatured, type I collagen substrata. Two IGD-containing type I modules are present within the %%%gelatin%%%-binding domain. The object of this study was to ascertain whether soluble synthetic peptides containing the IGD motif stimulate fibroblast migration. We found that IGD peptides stimulated fibroblast migration in the following order of activity: IGDS (as present in the ninth type I module) > IGDQ (as present in the seventh type I module) > IGD. The scrambled SDGI peptide and the well-characterised RGDS peptide were devoid of motogenic activity. The migratory response of fibroblasts to IGD-containing peptides consisted of two distinct phases: an initial period of peptide-mediated cell activation and a subsequent period of enhanced migration manifest in the absence of further IGD peptide. Cell activation was substratum-independent (occurring equally well on both native and denatured type I collagen substrata), whilst the manifestation of enhanced migration was persistent and substratum-dependent (being evident only by cells adherent to a native collagen substratum). Our data further indicated that cell activation (1) is elicited by a signal transduction cascade occurring within minutes of cell exposure to IGD-containing peptides, (2) is dependent upon integrin alphavbeta3 functionality, (3) involves the tyrosine phosphorylation of focal adhesion kinase (ppFAK125) and (4) is inhibited by signalling mediated through integrin alpha5beta1. The expression of migration stimulating activity by soluble IGD-containing peptides clearly distinguishes them from their %%%RGD%%% counterparts. This is the first identified biological activity of the highly conserved IGD motif and provides a rational platform for the development of a novel family of therapeutic compounds designed to stimulate cell migration in relevant clinical situations, such as impaired wound healing.

12/7/20
DIALOG(R)File 5:Biosis Previews(R)

14592310 BIOSIS NO.: 199800386557
The thrombospondin receptor CD47 (IAP) modulates and associates with alpha2beta1 integrin in vascular smooth muscle cells
AUTHOR: Wang Xue-Qing; Frazier William A (Reprint)
AUTHOR ADDRESS: Box 8231, Dep. Biochem. and Molecular Biophysics, Washington Univ. Sch. Med., 660 S. Euclid Ave., St. Louis, MO 63110, USA **USA
JOURNAL: Molecular Biology of the Cell 9 (4): p865-874 April, 1998 1998
MEDIUM: print
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The carboxyl-terminal domain of thrombospondin-1 enhances the migration and proliferation of smooth muscle cells. Integrin-associated protein (IAP or CD47) is a receptor for the thrombospondin-1 carboxyl-terminal cell-binding domain and binds the agonist peptide 4N1K (kRFYVVMWKk) from this domain. 4N1K peptide stimulates chemotaxis of both human and rat aortic smooth muscle cells on %%%gelatin%%%-coated filters. The migration on %%%gelatin%%% is specifically blocked by monoclonal antibodies against IAP and a beta1 integrin, rather than alphavbeta3 as found previously for 4N1K-stimulated chemotaxis of endothelial cells on %%%gelatin%%%. Both human and rat smooth muscle cells displayed a weak migratory response to soluble type I collagen; however, the presence of 4N1K peptide or intact thrombospondin-1 provoked a synergistic chemotactic response that was partially blocked by antibodies to alpha2 and beta1 integrin subunits and to IAP. A combination of antialpha2 and IAP monoclonal antibodies completely blocked chemotaxis. %%%RGD%%% peptide and antialphavbeta3 mAb were without effect. 4N1K and thrombospondin-1 did not augment the chemotactic response of smooth muscle cells to fibronectin, vitronectin, or collagenase-digested type I collagen. Complex formation between alpha2beta1 and IAP was detected by the coimmunoprecipitation of both alpha2 and beta1 integrin subunits with IAP. These data suggest that IAP can associate with alpha2,beta1 integrin and modulate its function.

12/7/21
DIALOG(R)File 5:Biosis Previews(R)

14384613 BIOSIS NO.: 199800178860
Small mechanical strains selectively suppress matrix metalloproteinase-1 expression by human vascular smooth muscle cells
AUTHOR: Yang Jeong-Hee; Briggs William H; Libby Peter; Lee Richard T (Reprint)
AUTHOR ADDRESS: Cardiovasc. Div., Brigham and Women's Hosp., 75 Francis St., Boston, MA 02115, USA**USA
JOURNAL: Journal of Biological Chemistry 273 (11): p6550-6555 March 13, 1998 1998
MEDIUM: print

ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mechanical forces and biochemical stimuli may interact to regulate cellular responses. In this study, we tested the hypothesis that very small mechanical strains interact with growth factors in the regulation of matrix metalloproteinase (MMP)-1. Human vascular smooth muscle cells (VSMCs) were cultured on a precoated silicone membrane in a device that imposes a highly uniform biaxial strain. VSMCs cultured on fibronectin were treated with cyclic 1-Hz strains of 0, 1, or 4%, and MMPs were assayed by Western analysis or %%%gelatin%%% zymography. Small strains did not induce MMP-1 in VSMCs, but strain was a potent inhibitor of platelet-derived growth factor (PDGF)- or tumor necrosis factor-a-induced synthesis of MMP-1. In contrast, MMP-2 and TIMP-2 levels were not changed by PDGF and/or mechanical strain. VSMCs strained on the 120-kDa chymotryptic fragment of fibronectin or %%%RGD%%% peptides suppressed PDGF-induced expression of MMP-1, indicating that this effect is not mediated by the heparin-binding domain or connecting segment-1 of fibronectin. Northern analysis of ets-1, a transcriptional activator of MMP-1 expression, showed that strain down-regulated ets-1 expression, whereas c-fos expression was augmented. Thus, small deformations can selectively suppress MMP-1 synthesis by VSMCs, demonstrating the exquisite sensitivity of the cell to mechanical stimuli.

14374692 BIOSIS NO.: 199800168939
A new pseudo-peptide of Arg-Gly-Asp (%%%RGD%%%) with inhibitory effect on tumor metastasis and enzymatic degradation of extracellular matrix
AUTHOR: Fujii Hideki; Nishikawa Naoyuki; Komazawa Hiroyuki; Suzuki Makoto; Kojima Masayoshi; Itoh Isamu; Obata Aya; Ayukawa Koichi; Azuma Ichiro; Saiki Ikuo (Reprint)
AUTHOR ADDRESS: Res. Inst. Wakan-Yaku, Toyama Med. Pharmaceutical Univ., 2630 Sugitani, Toyama 930-01, Japan**Japan
JOURNAL: Clinical and Experimental Metastasis 16 (1): p94-104 Jan., 1998
1998
MEDIUM: print
ISSN: 0262-0898
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A series of pseudo-peptide analogs of the Arg-Gly-Asp (%%%RGD%%%) sequence of fibronectin have been synthesized, and their anti-metastatic effects in mice and inhibitory effects on tumor cell invasion in vitro have been examined. The partially modified retro pseudo-peptide of %%%RGD%%%, Rrev-COCH2CO-D (FC-63), was more effective in inhibiting tumor metastasis than the original RGDS peptide. Replacement of the malonyl moiety of FC-63 with a carboxyethylene linkage (Rrev-COCH2CH2-D, FC-303) achieved more potent inhibition of lung metastasis of melanoma cells than FC-63. Among the analogs, FC-336, a p-xylylendiamine derivative having two FC-303 moieties, showed the most potent inhibitory effect on

experimental lung metastasis produced by i.v. co-injection with B16-BL6 melanoma or colon 26 M3.1 cells in a dose-dependent manner. Multiple administrations of FC-336 after tumor inoculation also showed efficient therapeutic potency against spontaneous lung metastasis of B16-BL6 melanoma in mice. Furthermore, FC-336 effectively inhibited the invasion, migration and adhesion of tumor cells in vitro, but its inhibitory effects were not more than those of RGDS peptide. Zymography analysis revealed that FC-336 inhibited the degradation of %%%gelatin%%% substrate by matrix metalloproteinases (MMPs) produced by tumor cells, while the RGDS peptide did not affect the enzymatic degradation. These findings indicate that the pseudo-peptides of the %%%RGD%%% sequence, possessing the inhibitory property of the degradation by MMPs differently from original %%%RGD%%%-containing peptides, may be advantageous and useful in preventing tumor metastasis.

12/7/23
DIALOG(R)File 5:Biosis Previews(R)

14373937 BIOSIS NO.: 199800168184
A new pseudo-peptide analogue of the Arg-Gly-Asp (%%%RGD%%%) sequence inhibits liver metastasis of colon 26-L5 carcinoma cells
AUTHOR: Ohnishi Yasuharu; Fuji Hideki; Murakami Koji; Sakamoto Takashi; Tsukada Kazuhiro; Fujimaki Masao; Kojima Masayoshi; Saiki Ikuo (Reprint)
AUTHOR ADDRESS: Dep. Pathogenic Biochem., Res. Inst. Wakan-yaku, Toyama Med. Pharm. Univ., 2630 Sugitani, Toyama 930-01, Japan**Japan
JOURNAL: Cancer Letters 124 (2): p157-163 Feb. 27, 1998 1998
MEDIUM: print
ISSN: 0304-3835
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have investigated the effect of the pseudo-peptide analogue (FC-336) of the Arg-Gly-Asp (%%%RGD%%%) sequence in a liver metastasis model by the inoculation of a highly liver-metastatic cell line of colon 26 carcinoma (colon 26-L5) into the portal vein of BALB/c mice. The intraportal injection of colon 26-L5 cells with FC-336 resulted in a marked suppression of liver metastatic colonies in a dose-dependent manner and it reduced the liver weights to a normal level. However, the co-injection of tumor cells with a high dose of RGDS tetrapeptide led to a slight inhibition of liver metastasis. The multiple i.v. administration of FC-336 after tumor inoculation as well as the injection of FC-336 with tumor cells caused significant inhibition of experimental metastasis in the liver. The multiple i.v. administration of the RGDS peptide did not show any inhibitory activity. FC-336 significantly enhanced the survival rate of mice compared with untreated controls when injected intraportally with tumor cells or when intravenously administered after tumor inoculation. Zymography analysis showed that FC-336 inhibited the degradation of %%%gelatin%%% substrate by matrix metalloproteinases (MMPs) produced by colon 26-L5 cells, while RGDS peptide did not affect the enzymatic degradation. These findings clearly indicate that the pseudo-peptides of the %%%RGD%%% sequence (FC-336) have a potent inhibitory activity on liver metastasis of colon 26-L5 carcinoma cells.

12/7/24
DIALOG(R)File 5:Biosis Previews(R)

13262184 BIOSIS NO.: 199698730017
Specific sequences of fibronectin activate the protein kinase C signal transduction pathway in invasive bladder cancer
AUTHOR: Margolis Eric J; Choi Jimmy C S; Shu Wei-Ping; Liu Brian C-S (Reprint)
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JOURNAL: Cancer Letters 100 (1-2): p163-168 1996 1996
ISSN: 0304-3835
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The mechanism of human bladder cancer cell invasion is not clear, but it appears that extracellular matrix components, such as fibronectin, may be involved. To investigate the role of fibronectin in tumor cell invasion and progression, we used an in vitro invasion assay to define the motility stimulating fragment of fibronectin for invasive human bladder cancer T24 cells. Using a modified Boyden chamber assay and purified fragments of fibronectin, we demonstrated that both the 120 kDa chymotrypsin generated fragment of fibronectin (containing the cell attachment %%%RGD%%% motif and additional sequences towards the carboxyl-terminal heparin binding domain), as well as the trypsin generated 60 kDa fragment of fibronectin (containing the carboxyl-terminal heparin binding domain and additional sequences towards the cell attachment %%%RGD%%% motif), were able to stimulate the migration of invasive human bladder cancer T24 cells. Control fragments containing only the amino-terminal %%%gelatin%%% binding region of fibronectin did not stimulate the motility of the human bladder cancer T24 cells. To determine the molecular mechanism in which these fragments may stimulate the migration of the T24 cells, we assayed for intracellular signal transduction pathway protein kinase C (PKC). We demonstrated that both the 120 kDa and the 60 kDa fragments were able to stimulate the activation of protein kinase C. Non-motility stimulating fragments of fibronectin were not able to activate protein kinase C. We conclude that the PKC signal transduction pathway may be involved in matrix mediated motility, and suggest that the inhibition of such pathway(s) may alter the malignant phenotype of human bladder cancer.

12/7/25
DIALOG(R)File 5:Biosis Previews(R)

13182414 BIOSIS NO.: 199698650247
Adherence, fibronectin binding, and induction of cytoskeleton reorganization in cultured human cells by Mycoplasma penetrans
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JOURNAL: Infection and Immunity 64 (1): p197-208 1996 1996
ISSN: 0019-9567
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mycoplasma penetrans adhered to cultured human cells, forming clusters that localized to specific areas of the host cell surface. Adherence and cluster formation were inhibited by anti-M. penetrans antibodies, suggesting the involvement of specific adhesin-receptor interactions. Ultrastructural studies showed that after 2 h of infection, mycoplasmas attach to and penetrate the host cell surface. M. penetrans bound selectively to immobilized fibronectin, an interaction which was not inhibited by a 70-kDa fragment containing a heparin-%%%gelatin%%% -binding domain of fibronectin, other matrix glycoproteins, or an %%%RGD%%% tripeptide, suggesting the recognition of other specific binding sites on the fibronectin molecule. A ca. 65-kDa fibronectin-binding protein of M. penetrans was eluted following Sepharose-fibronectin affinity chromatography. Confocal, light, and immunofluorescence microscopy demonstrated that the interaction of M. penetrans with target cells triggers a signal that causes recruitment of several cytoskeletal components, including tubulin and alpha-actinin, and aggregation of phosphorylated proteins. Detergent-soluble mycoplasma proteins with apparent molecular masses of 18, 28, 32, 36, 39, and 41 kDa selectively bound to glutaraldehyde-fixed HEp-2 cells. Our findings offer new insights into understanding the interaction of this human mycoplasma with host target cells.

12/7/26
DIALOG(R)File 5:Biosis Previews(R)

13027722 BIOSIS NO.: 199598495555
Release of biological activities from quiescent fibronectin by a conformational change and limited proteolysis by matrix metalloproteinases
AUTHOR: Fukai Fumio (Reprint); Ohtaki Mitsuru; Fujii Nozomi; Yajima Hirofumi; Ishii Tadahiro; Nishizawa Yoshinori; Miyazaki Kaoru; Katayama Takashi
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JOURNAL: Biochemistry 34 (36): p11453-11459 1995 1995
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We reported that specific biological activities are confined to three domains of the fibronectin (Fn) molecule (Fukai et al. (1991) J. Biol. Chem. 266, 8807; Fukai et al. (1993) Biochemistry 32, 5746): the potent ability to stimulate the adipocyte differentiation of ST-13 cells is in the amino-terminal fibrin-binding (Fib 1) domain (referred to as Fib 1 domain activity); the %%%RGD%%%-dependent activities that stimulate NIH-L13 cell migration and inhibit adipocyte differentiation are in the central cell-binding (Cell) domain (Cell domain activity); and the activity that stimulates cell migration in a %%%RGD%%%-independent manner is in the carboxyl-terminal fibrin-binding (Fib 2) domain (Fib 2 domain activity). Human plasma Fn which was purified without exposure to a denaturant, such as urea, exhibited no Fib 1, Fib 2, or Cell domain

activity. By exposure to urea or surface adsorption, Fn showed Cell domain activity but not those of the Fib 1 and Fib 2 domains. Whether the cryptic domain activities are disclosed or not depended on whether or not the responsible domains were irreversibly exposed from confined environments of Fn structure as confirmed by light-scattering measurement and enzyme immunoassay using domain-specific monoclonal antibodies. We then investigated the action of matrix metalloproteinases (MMPs) in liberating the Fib 1, Cell, and Fib 2 domain activities. Matrilysin released only the Cell domain activity. In contrast, stromelysin, collagenase, and especially %%%gelatinase%%% A additionally liberated the Fib 1 and Fib 2 domain activities. The Fib 1, Fib 2, and Cell domains acquired much higher activities when they were freed from linkage with adjacent domains. The results suggested that the Fib 1, Cell, and Fib 2 domains are buried in the native Fn structure, but are disclosed via two separate routes: the Cell domain activity is exposed by a conformational change and the others by proteolytic fragmentation.

12951560 BIOSIS NO.: 199598419393
Identification of integrins involved in cell adhesion to native and denatured type I collagens and the phenotypic transition of rabbit arterial smooth muscle cells
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JOURNAL: Experimental Cell Research 219 (1): p249-256 1995 1995
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Rabbit smooth muscle cells (SMC) in primary culture attached to and started proliferating on native and heat-denatured type I collagens, although the amount of cell attachment to denatured collagen was significantly lower. The cells adhered poorly and were unable to grow on commercial %%%gelatin%%%. In contrast, synthetic SMC in secondary culture could adhere to %%%gelatin%%% and grew as well on %%%gelatin%%% as on native type I collagen. The SMC in the contractile state adhered to native type I collagen through the alpha-1-beta-1 and alpha-3-beta-1 integrins. The cells in the intermediate phenotype also adhered to the substrate through the alpha-1-beta-1 and alpha-3-beta-1 integrins, but the relative amount of a3 integrin decreased. The initial adhesion of cells in secondary culture to native type I collagen was mediated only by the alpha-1-beta-1 integrin. The cell-binding sequences did not contain DGEA (Asp-Gly-Glu-Ala) or %%%RGD%%% (Arg-Gly-Asp). In contrast, cell adhesion to heat-denatured type I collagen was mediated only by the a1-beta-1 integrin in the contractile state and by the alpha-1-beta-1, alpha-2-beta-1, and alpha-3-beta-1 integrins in the synthetic state. In heat-denatured type I collagen, the sequences DGEA and %%%RGD%%% served as a recognition site for the alpha-2-beta-1 and alpha-3-beta-1 integrins. Our results suggest that rabbit SMC can recognize the native and denatured type I collagens through interactions with the triple

helix-binding receptors and a chain-binding receptors and that the expression pattern of integrins changes in conjunction with the phenotypic properties of vascular SMC.

12/7/28
DIALOG(R)File 5:Biosis Previews(R)

12844557 BIOSIS NO.: 199598312390
Cooperative Signaling by alpha-5-beta-1 and alpha-4-beta-1 Integrins Regulates Metalloproteinase Gene Expression in Fibroblasts Adhering to Fibronectin
AUTHOR: Huhtala Pirkko (Reprint); Humphries Martin J; McCarthy James B; Tremble Patrice M; Werb Zena; Damsky Caroline H
AUTHOR ADDRESS: HSW 604, Dep. Stomatol., 513 Parnassus Ave., Univ. California, San Francisco, CA 94143-0512, USA**USA
JOURNAL: Journal of Cell Biology 129 (3): p867-879 1995 1995
ISSN: 0021-9525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Rabbit synovial fibroblasts (RSF) express basal levels of the metalloproteinases (MMP) collagenase, stromelysin-1 and 92-kD %%%gelatinase%%% when plated on intact fibronectin (FN), but elevated levels when plated on either the central %%%RGD%%%-containing cell-binding region of FN (120FN) or antibody against the alpha-5-beta-1 integrin, suggesting that domains outside 120FN may suppress the induction of MMP (Werb, Z., P. M. Tremble, O. Behrendtsen, E. Crowley, and C. H. Damsky. 1989. J. Cell Biol. 109:877-889). We therefore attempted to reconstitute the basal signaling of intact FN by plating RSF on 120FN together with domains of FN outside this region. Large COOH-terminal fragments containing both the heparin-binding and IIICS domains suppressed MMP when combined with 120FN. To map the active sequences, peptides from this region and larger fragments that did, or did. not, include the CS-1 portion of IIICS were tested. Only CS-1 peptide, or larger fragments containing CS-1, suppressed MMP expression induced by 120FN. In contrast, peptide V from the heparin-binding region, shown previously to stimulate focal contact formation, further enhanced MMP expression by RSF when present on the substrate with 120FN. RSF expressed alpha-4-beta-1 integrin, the receptor for CS-1, and the anti-alpha-4 mAb blocked the ability of CS-1 to suppress MMP induction by 120FN. These results show that signals modulating MMP expression and focal contact assembly are regulated independently, and that cooperative signaling by alpha-5-beta-1 and alpha-4-beta-1 integrins plays a dominant role in regulating expression of these extracellular matrix-remodeling genes in response to FN. This work demonstrates directly the modular way in which information in the extracellular matrix is detected and processed by cell surface receptors.

12/7/29
DIALOG(R)File 5:Biosis Previews(R)

12720411 BIOSIS NO.: 199598188244

Binding of plasma fibronectin to Candida albicans occurs through the cell binding domain
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JOURNAL: Microbial Pathogenesis 17 (6): p387-393 1994 1994
ISSN: 0882-4010
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Candida albicans yeast cells bind soluble human plasma fibronectin (Fn) through a glycoprotein receptor (adhesin) located on the cell surface. This work demonstrates that a 120 kDa proteolytic fragment of Fn encompassing the cell binding domain binds more avidly to the yeast cell adhesin than does the parent Fn molecule. The presence of binding of Fn fragments containing heparin- and %%%gelatin%%%-binding domains of Fn could not be detected. The binding of the 120 kDa fragment is inhibited by a monoclonal antibody to the cell binding domain containing the amino acid sequence, Arginine-Glycine-Aspartic acid (%%%RGD%%%) as well as by an %%%RGD%%%-containing apprx 23-mer Fn peptide, but not with heparin or GRGDSPL. The fact that the cell binding domain of soluble Fn binds more avidly than does the parent molecule may explain the difference in the interaction of soluble Fn and immobilized Fn with Candida. It is possible that, upon immobilization, Fn may expose domains of the molecule previously unexposed when the molecule is in the soluble state.

12/7/30
DIALOG(R)File 5:Biosis Previews(R)

12178461 BIOSIS NO.: 199497199746
Use of recombinant and synthetic peptides as attachment factors for cells on microcarriers
AUTHOR: Varani James (Reprint); Inman Dennis R; Fligiel Suzanne E G; Hillegas William J
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JOURNAL: Cytotechnology 13 (2): p89-98 1993 1993
ISSN: 0920-9069
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Polystyrene culture dishes and polystyrene microcarriers were coated with Pronectin-F and poly-L-lysine (polylysine), either alone or in combination. Pronectin-F is a recombinant peptide containing repeats of the %%%RGD%%% cell-attachment sequence from fibronectin. Polylysine is a polymer of L-lysine. Pronectin-F supported attachment of Madin-Darby Canine Kidney (MDCK) cells at concentrations as low as 0.025 mu-g/cm-2 of surface area. The cells rapidly spread after attachment. Polylysine at concentrations of 0.05-0.5 mu-g/cm-2 also supported cell attachment but cells did not rapidly spread after attachment to this substrate. Higher concentrations of polylysine could not be used because of toxicity. When the two peptides were used in conjunction, MDCK cells attached and spread at lower peptide concentrations than they did when either substrate was

used alone. These findings suggest that recombinant Pronectin-F alone or in conjunction with a cationic polymer could be a useful replacement for materials such as %%%gelatin%%% or collagen which are currently used as microcarrier surfaces.

12/7/31
DIALOG(R)File 5:Biosis Previews(R)

11836357 BIOSIS NO.: 199396000773
Platelet interactions with fibronectin: Divalent cation-independent platelet adhesion to the %%%gelatin%%%-binding domain of fibronectin
AUTHOR: Winters Kenneth J; Walsh John J; Rubin Brian G; Santoro Samuel A (Reprint)
AUTHOR ADDRESS: Dep. Pathol., Box 8118, Washington University Sch. Med., St. Louis, MO 63110, USA**USA
JOURNAL: Blood 81 (7): p1778-1786 1993
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Divalent cation-dependent platelet adhesion to fibronectin (FN) is mediated by the integrin receptors alpha-5-beta-1 (GP Ic-IIa) and alpha-IIb-beta-3 (GP IIb-IIIa), which recognize the %%%RGD%%% (Arg-Gly-Asp) sequence in the cell-binding domain. However, FN can also support divalent cation-independent platelet adhesion. To determine which domain of FN mediates divalent cation-independent adhesion, proteolysis with thermolysin and affinity chromatography were used to isolate the cell-binding, %%%gelatin%%%-binding, and heparin-binding domains of FN. Unactivated and thrombin-activated platelets adhered to intact FN and the 45-Kd %%%gelatin%%%-binding domain in the presence of either Ca-2+ or EDTA. Platelet spreading was mediated only by the 105-Kd cell-binding domain and required divalent cations. The heparin-binding domains did not support platelet adhesion. Reduction of intrachain disulfide bonds or removal of carbohydrate side chains on the %%%gelatin%%%-binding domain did not alter the ability to support platelet adhesion. Divalent cation-independent adhesion to the 45-Kd %%%gelatin%%%-binding domain was not inhibited by RGDS (Arg-Gly-Asp-Ser) synthetic peptides or monoclonal antibodies (MoAbs) directed against known platelet receptors. We conclude that platelets can adhere but not spread on the %%%gelatin%%%-binding domain of FN by a novel divalent cation-independent mechanism.

12/7/32
DIALOG(R)File 5:Biosis Previews(R)

11361011 BIOSIS NO.: 199294062852
MECHANISM OF HUMAN KERATINOCYTE MIGRATION ON FIBRONECTIN UNIQUE ROLES OF %%%RGD%%% SITE AND INTEGRINS
AUTHOR: KIM J P (Reprint); ZHANG I; CHEN J D; WYNN K C; KRAMER R H; WOODLEY D T
AUTHOR ADDRESS: DEP DERMATOL, STANFORD UNIV SCH MED, STANFORD, CALIF 94305, USA**USA
JOURNAL: Journal of Cellular Physiology 151 (3): p443-450 1992

ISSN: 0021-9541
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The migration of human keratinocytes over the wound bed plays an important role in the re-epithelialization of cutaneous wounds. Fibronectin, a large glycoprotein matrix component that is abundant within cutaneous wound beds, promotes keratinocyte migration. However, the mechanisms by which keratinocytes migrate over fibronectin are unknown. In this study, we sought to identify specific sites within the fibronectin molecule that induce keratinocyte locomotion and to characterize the cell surface receptors involved. The data show that the domain within the fibronectin molecule that induces human keratinocyte migration is the 120 kD cell-binding domain close to the carboxyl terminus. The 40 kD heparin-binding domain near the carboxyl terminus and the 45 kD %%%gelatin%%%-binding domain near the amino terminus did not promote keratinocyte migration. In addition, keratinocyte migration on both fibronectin and the 120 kD cell-binding domain was completely inhibited by the presence of GRGDSP peptide, suggesting that keratinocyte migration on fibronectin is mediated by recognizing the %%%RGD%%% sequence located within the cell-binding domain of fibronectin. Furthermore, keratinocytes were able to migrate directly on immobilized %%%RGD%%% substratum. Cell migration on fibronectin is mediated by the .alpha.5.beta.1 integrin since antibodies blocking the .alpha.5 and the .beta.1 subunits completely inhibited keratinocyte migration on fibronectin. In addition, we demonstrate that human keratinocytes express .alpha.5.beta.1 integrin in culture by flow cytometry.

11357970 BIOSIS NO.: 199294059811
SPREADING OF HELA CELLS ON A COLLAGEN SUBSTRATUM REQUIRES A SECOND MESSENGER FORMED BY THE LIPOXYGENASE METABOLISM OF ARACHIDONIC ACID RELEASE BY COLLAGEN RECEPTOR CLUSTERING
AUTHOR: CHUN J-S (Reprint); JACOBSON B S
AUTHOR ADDRESS: DEP BIOCHEM AND MOL BIOL, PROGRAM MOL AND CELL BIOL, UNIV MASS, AMHERST, MASS 01003, USA**USA
JOURNAL: Molecular Biology of the Cell 3 (5): p481-492 1992
ISSN: 1059-1524
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: HeLa cells attach to a variety of substrata but spread only on collagen or %%%gelatin%%%. Spreading is dependent on collagen-receptor upregulation, clustering, and binding to the cytoskeleton. This study examines whether second messengers are involved in initiating the spreading process on %%%gelatin%%%. The levels of cytosolic free calcium ([Ca++]i), cAMP, and cytoplasmic pH (pHi) do not change during cell attachment and spreading. However, a basal level of [Ca++]i and an alkaline pHi are required for spreading. There is an activation of protein kinase C (PKC) and a release of arachidonic acid (AA) on attachment and before cell spreading. Inhibition of PKC does not block

cell spreading, indicating that PKC activation is not essential for spreading. Inhibition of phospholipase A2 blocks cell spreading, whereas addition of exogeneous AA overcomes this inhibitory effect. Among AA metabolic pathways, inhibitors of lipoxygenase (LOX) block cell speading, suggesting that a LOX product(s) formed from AA initiates spreading. Clustering receptors for collagen with polyclonal antibodies, or with anti-collagen-receptor antigen-binding fragments (Fab) in combination with a secondary antibody, induce AA release. Also, AA is released when cells attach to either immobilized %%%gelatin%%% or immobilized Arg-Gly-Asp (%%%RGD%%%) peptide. Thus, AA is released whenever receptor clustering is observed. Receptor occupancy is not sufficient to release AA; when cells are treated with %%%gelatin%%% or %%%RGD%%% peptide in solution or anti-collagen-receptor Fab fragments without secondary antibody, conditions where receptor clustering is not observed, AA is not released. Thus, a LOX metabolite(s) of AA formed by collagen-receptor clusering is a second messenger(s) that initiates HeLa cell spreading. LOX inhibitors also block the spreading of bovine aortic endothelial cells, chicken embryo fibroblasts, and CV-1 fibroblasts on %%%gelatin%%% or fibronectin, indicating that other cells might use the same second messenger system in initiating cell-substratum adhesion.

11338345 BIOSIS NO.: 199294040186
ACTIVATED T LYMPHOCYTES AND MACROPHAGES SECRETE FIBRONECTIN WHICH STRONGLY SUPPORTS CELL ADHESION
AUTHOR: HERSHKOVIZ R (Reprint); ALON R; GILAT D; LIDER O
AUTHOR ADDRESS: DEP CELL BIOL, R326, WEIZMANN INST SCI, PO BOX 26, REHOVOT 76100, ISRAEL**ISRAEL
JOURNAL: Cellular Immunology 141 (2): p352-361 1992
ISSN: 0008-8749
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Matrix-bound fibronectin (FN) appears to be involved in cell adhesion and motility mediated by integrin receptors. Although lymphoid cells and other cell types are capable of producing and secreting FN, the precise role of this secreted FN-like factor in regulating immune reactions is unclear. In the present study we analyzed the adhesive properties of FN secreted by rat CD4+ T cells and clone cells activated by the T cell mitogen concanavalin A (Con A), antigen, or via the CD2 pathways, or by macrophages (M.vphi.) activated by lipopolysaccharide (LPS). Immobilized culture supernatant (CS) from the activated T cells of M.vphi. supports the adhesion of activated rat or human CD4+ T cell or murine tumor cell. These CS contained FN and were more potent at facilitating cell adhesion then plasma FN. The adhesion activity of CS was attributed to FN because (a) %%%gelatin%%% columns depleted the FN present in the CS and (b) pretreating the cells with peptides of the cell-binding domain of FN aborgated their ability to bind CS. CS-mediated adhesion appears to occur primarily via the recognition of the Arg-Gly-Asp (%%%RGD%%%) by the .beta.1-integrin-specific receptors of the adhesive cells. Thus, we postulate that FN secreted by various types of leukocytes is involved in promoting essential cell-matrix intractions,

possibly affecting cell-adhesive and migratory processes at inflammatory or extravasation sites.

12/7/35
DIALOG(R)File 5:Biosis Previews(R)

11175356 BIOSIS NO.: 199293018247
SULFHYDRYL-DEPENDENT ATTACHMENT OF TREPONEMA-DENTICOLA TO LAMININ AND OTHER PROTEINS
AUTHOR: HAAPASALO M (Reprint); SINGH U; MCBRIDE B C; UITTO V-J
AUTHOR ADDRESS: DEP ORAL BIOLOGY, UNIVERSITY BRITISH COLUMBIA, VANCOUVER, BRITISH COLUMBIA V6T1Z3, CAN**CANADA
JOURNAL: Infection and Immunity 59 (11): p4230-4237 1991
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Attachment of Treponema denticola ATCC 35405 to laminin, a major basement membrane protein, and to other proteins was studied. Microdilution plates were coated with the proteins, and the attachment of T. denticola was measured by the enzyme-linked immunosorbent assay technique. Compared with bovine serum albumin (BSA), T. denticola had a high affinity to laminin, fibronectin, fibrinogen, and %%%gelatin%%%, as well as to type I and type IV collagens. Attachment to %%%RGD%%% peptide (Gly-Arg-Gly-Asp-Ser, the integrin recognition sequence) was only about 30% of that to laminin and was comparable to attachment to BSA. Tests with laminin fragments obtained through elastase digestion showed that the spirochetes attached well to an A-chain 140-kDa fragment involved in eukaryote cell attachment but did not attach to a 50-kDa fragment that includes the heparin binding site. Pretreatment of T. denticola with soluble laminin, fibronectin, %%%gelatin%%%, BSA, or fibrinogen had no effect on the attachment of the bacteria to laminin or fibronectin. A wide variety of compounds were tested for their possible inhibitory actions on the attachment. While most treatments of T. denticola ATCC 35405 had little or no effect on the attachment to proteins, sulfhydryl reagents p-chloromercuribenzoic acid (pCMBA) and oxidized glutathione inhibited the attachment by 70 to 99%, depending on the protein. When T. denticola was first allowed to attach to proteins, addition of pCMBA or oxidized glutathione could no longer reverse the attachment. Heat treatment of the spirochetes also markedly reduced the attachment to laminin, %%%gelatin%%%, and fibrinogen but not to BSA. Mixed glycosidase treatment of the spirochetes inhibited the attachment by 20 to 80%. None of the above treatments of the substrate proteins had any marked effect on the spirochete attachment. The results indicate that T. denticola has the capacity to bind to many different kinds of proteins by utilizing specific attachment mechanisms. The binding appears to involve protein SH groups and/or carbohydrate residues on the surface of T. denticola.

12/7/36
DIALOG(R)File 5:Biosis Previews(R)

10879258 BIOSIS NO.: 199192125029

FIBRONECTIN FRAGMENTS RELEASES FROM PHORBOL ESTER-STIMULATED PULMONARY ARTERY ENDOTHELIAL CELL MONOLAYERS PROMOTE NEUTROPHIL CHEMOTAXIS
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JOURNAL: Immunology 74 (1): p114-120 1991
ISSN: 0019-2805
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have recently shown that monolayer cultures of calf pulmonary artery endothelial (CPAE) cells pretreated with phorbol myristate acetate (PMA) generate a conditioned medium that is chemotactic for human polymorphonuclear leucocytes (PMNL). Fibronectin (Fn) is a multidomain protein found in the plasma and subendothelial extracellular matrix that induces attachment and migration of a variety of cell types. The present study was designed to evaluate the role of Fn or fragments of Fn present in conditioned medium from phorbol ester-stimulated endothelial cells as potential chemotactic factors for human PMNL. A large number of Fn fragments were revealed by Western immunoblotting of serum-free conditioned medium 4 hr after treatment of CPAE monolayers with PMA. %%%Gelatin%%%-Sepharose affinity chromatography of 4-hr conditioned medium demonstrated chemotactic activity for PMNL in both %%%gelatin%%% -binding and non-%%%gelatin%%%-binding fractions. The addition of bovine Fn antiserum to the conditioned medium inhibited PMNL chemotaxis in a dose-dependent manner while having no effect on PMNL chemotaxis generated by zymosan-activated serum. One site on the Fn molecule known to interact with phagocytic cells is the cell-binding domain containing the Arg-Gly-Asp (%%%RGD%%%) sequence. Pretreatment of PMNL with a %%%RGD%%% -containing peptide (1 mM GRGDSPK) for 10 min completely inhibited the expression of chemotactic activity present in conditioned medium and in the %%%gelatin%%%-binding and non-%%%gelatin%%%-binding fractions. PMNL chemotaxis was not stimulated by either intact Fn or the %%%RGD%%% -containing septapeptide tested over a wide concentration range. However, incubation of PMNL with a purified 120,000-MW fragment of Fn containing the cell-binding domain stimulated chemotaxis in a dose-dependent manner. In contrast, a purified 45,000 MW fragment of Fn containing the %%%gelatin%%%-binding domain was not chemotactic for PMNL. When a monoclonal antibody directed against the cell-binding domain of Fn was incubated with conditioned medium, a significant reduction in PMNL chemotaxis was observed. These results demonstrate that phorbol ester-stimulated pulmonary artery endothelial cells release Fn fragments and suggest an important role for Fn fragments containing the cell-binding domain in stimulating the migration of PMNL.

12/7/37

10850306 BIOSIS NO.: 199192096077
RECRUITMENT OF PERIPHERAL MONONUCLEAR CELLS BY MAMMALIAN COLLAGENASE DIGESTS OF TYPE I COLLAGEN
AUTHOR: MALONE J D (Reprint); RICHARDS M; JEFFREY J J
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JOURNAL: Matrix 11 (4): p289-295 1991
ISSN: 0934-8832
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Type I collagen is highly susceptible to proteolytic cleavage by neutral mamalian collagenase. Following an initial site specific cleavate of the substrate, two characteristic products are generated, TCA and TCB. These two products then spontaneously denature and are degraded into multiple smaller molecular weight peptides. We prepared TCA and TCB from native type I collagen by the action of rat uterine fibroblast neutral collagenase. In addition we prepared denatured type I .alpha. chains and exposed them to the action of collagenase under controlled conditions in order to generate small molecular weight peptides. We then examined intact type I collagen. TCA and TCB and type I %%%gelatin%%% peptides for chemotactic activity in a Boyden chamber assay using both human peripheral monocytes and polymorphonuclear leucocytes as target cells. Intact type I collagen, while chemotactic for neutrophils, failed to elicit any chemotactic response in mononuclear cells. In addition, the results demonstrate an absence of any detectable chemotactic activity for either TCA or TCB when human peripheral monocytes were used as the target cells. However, type I collagen peptides demonstrated chemotactic activity for peripheral monocytes. Maximum cell migration was found with digests which had been exposed to neutral mammalian collagenase for three to four hours. No chemotractic activity was found using the same peptides, when neutrophils were used as the target cells. The data strongly suggest that chemotactic activity for mononuclear cells, normally suppressed in intact type I collagen, is revealed and/or activated by neutral collagenase digestion. Conversely, chemotactic activity for neutrophils is lost when intact type I collagen is digested into smaller molecular weight fragments. To further examine the mechanism(s) of the directed migratory response to collagen peptides, we used the ubiquitous extracellular matrix tripeptide, ARG-GLY-ASP, present in type I collagen, to probe the chemotactic response to type I %%%gelatin%%% peptides. Arg-Gly-Asp had no intrinsic agonist activity. Co-incubation peripheral mononuclear cells with Arg-Gly-Asp did not block the cell migration response to collagen peptides. These latter observations demonstrate that %%%RGD%%% is not critical for monocyte migration to type I collagen peptides.

12/7/38
DIALOG(R)File   5:Biosis Previews(R)

10633608   BIOSIS NO.: 199191016499
PLATELET C1Q RECEPTOR INTERACTIONS WITH COLLAGEN AND C1Q-COATED SURFACES
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JOURNAL: Journal of Immunology 145 (9): p2984-2988 1990
ISSN: 0022-1767
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RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We recently described specific binding sites for C1q on human blood platelets. Structural similarities between the amino-terminal of C1q and collagen have suggested that receptors for both molecules on platelets might be the same. The present study thus compared the interaction of purified C1q receptors (C1qR) and whole platelets with collagen- and C1q-coated polystyrene surfaces. Surfaces coated with BSA or %%%gelatin%%% served as controls. Purified 125I-labeled C1qR recognized both C1q- and collagen-coated surfaces in a divalent, cation-dependent manner. This adhesion was inhibited by polyclonal or monoclonal (II1/D1) anti-C1qR antibodies. Although C1qR adhered preferentially to C1q-coated surfaces, adhesion to bovine and human type I collagen, as well as to human type III and V collagen, was also noted. In parallel studies, 51Cr-labeled platelets bound equally well to collagen- or C1q-coated surfaces, albeit in a magnesium-dependent manner. Partial inhibition of platelet adhesion was observed in the presence of RGDS, despite the inability of RGDS to modify C1qR interaction with C1q or collagen. Moreover, anti C1qR antibodies selectively inhibited platelet adhesion to C1q-coated surfaces, whereas antibodies specific for the GPIa/IIa collagen receptor (6F1) preferentially inhibited platelet collagen interactions. These data support the presence or distinct platelet membrane C1qR, which may cross-react with collagen, and suggest that C1qR are necessary but not sufficient for platelet adhesion to C1q-coated surfaces. Additional divalent cation and/or %%%RGD%%% -sensitive binding sites may participate.

10188709 BIOSIS NO.: 199089106600
INHIBITION OF TUMOR-CELL ATTACHMENT TO EXTRACELLULAR MATRIX AS A METHOD FOR PREVENTING TUMOR RECURRENCE IN A SURGICAL WOUND
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JOURNAL: Annals of Surgery 210 (6): p758-764 1989
ISSN: 0003-4932
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Studies with four different transplantable murine tumors demonstrated that surgical instruments contaminated by contact with a tumor mass could produce tumors in a surgical wound. Eighty-seven per cent of mice with wounds made by invisibly contaminated scissors developed tumors. Irrigation with water did not prevent tumor growth. Before spilled tumor cells can invade and grow into a recurrence in the wound site, they must first attach to underlying extracellular matrix. We have devised a simple in vitro assay to identify inhibitors of tumor-cell attachment to develop therapeutic compounds that can prevent tumor-cell reimplantation. Various test compounds, including proteases (trypsin and Dispase), known modulators of matrix metabolism (proline analogues, cycloheximide, heparin, cortisone, cortexolone, and heparin-steroid combinations), large molecular weight polymers (agarose, dextran, polyethylene oxide), and synthetic fibronectin peptides were tested for their ability to inhibit mouse melanoma (B16-F10) cell attachment to

%%%gelatinized%%% dishes. Most of these compounds had little or no effect on tumor-cell adhesion when cells were plated in serum-containing medium. However we identified three compounds that inhibited tumor-cell attachment in a reversible fashion: (1) a specific inhibitor of collagen deposition (L-azetidine-2-carboxylic acid); (2) a bacterial neutral protease (Dispase); and (3) synthetic fibronectin peptides that contained the arginine-glycine-asparate (%%%RGD%%%) sequence that is responsible for cell binding. Dispause and the %%%RGD%%%-containing peptides also inhibited cell implantation and prevented tumor formation in a surgical wound. We propose that inhibitors of attachment might be used either alone or with other biologic modifiers to prohibit implantation of free tumor cells at the time of surgery and thus, to prevent local tumor recurrence.

12/7/40
DIALOG(R)File 5:Biosis Previews(R)

10132905 BIOSIS NO.: 199089050796
INHIBITION OF TUMOR-CELL ATTACHMENT TO EXTRACELLULAR MATRIX AS A METHOD FOR PREVENTING TUMOR RECURRENCE IN A SURGICAL WOUND
AUTHOR: WHALEN G F (Reprint); INGBER D E
AUTHOR ADDRESS: DEP SURGERY, NEW YORK HOSPITAL-CORNELL UNIV MED CENTER, 525 EAST 68TH ST, NEW YORK, NY 10021, USA**USA
JOURNAL: Annals of Surgery 210 (6): p758-764 1989
ISSN: 0003-4932
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Studies with four different transplantable murine tumors demonstrated that surgical instruments contaminated by contact with a tumor mass could produce tumors in a surgical wound. Eighty-seven per cent of mice with wounds made by invisibly contaminated scissors developed tumors. Irrigation with water did not prevent tumor growth. Before spilled tumor cells can invade and grow into a recurrence in the wound site, they must first attach to underlying extracellular matrix. We have derived a simple in vitro assay to identify inhibitors of tumor-cell attachment to develop therapeutic compounds that can prevent tumor-cell reimplantation. Various test compounds, including proteases (trypsin and Dispase), known modulators of matrix metabolism (proline analogues, cycloheximide, heparin, cortisone, cortexolone, and heparin-steroid combinations), large molecular weight polymers (agarose, dextran, polyethylene oxide), and synthetic fibronectin petides were tested for their ability to inhibit mouse melanoma (B16-F10) cell attachment to %%%gelatinized%%% dishes. Most of these compounds had little or no effect on tumor-cell adhesion when cells were plated in serum-containing medium. However, we identified three compounds that inhibited tumor-cell attachment in a reversible fashion: (1) a specific inhibitor of collagen deposition (L-azetidine-2-carboxylic acid); (2) a bacterial neutral protease (Dispae); and (3) synthetic fibronectin peptides that contained the arginine-glycine (%%%RGD%%%) sequence that is responsible for cell binding. Dispase and the %%%RGD%%%-containing peptides also inhibited cell implantation and prevented tumor formation in a surgical wound. We propose that inhibitors of attachment might be used either alone or with other biologic modifiers to prohibit implantation of free tumor cells at

the time of surgery and thus, to prevent local tumor recurrence.

12/7/41
DIALOG(R)File 5:Biosis Previews(R)

09708226 BIOSIS NO.: 198988023341
HUMAN MICROVASCULAR ENDOTHELIAL CELLS EXPRESS INTEGRIN-RELATED COMPLEXES THAT MEDIATE ADHESION TO THE EXTRACELLULAR MATRIX
AUTHOR: CHENG Y-F (Reprint); KRAMER R H
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JOURNAL: Journal of Cellular Physiology 139 (2): p275-286 1989
ISSN: 0021-9541
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Microvascular endothelial cells (MEC) must use a set of surface receptors to adhere not only to the vascular basement membrane but, during angiogenic stimulation, to the interstitum. We examined how cultured MEC isolated from human foreskin interact with their subendothelial matrix. MEC were able to attach to diverse extracellular matrix proteins, including fibronectin (Fn), vitronectin (Vn), laminin (Ln), type I and IV collagent, as well as to fibrinogen and %%%gelatin%%% . Adhesion to Fn, but not to laminin or collagens, was specifically blocked in the presence of Arg-Gly-Asp (%%%RGD%%%)-containing peptides. When surface radioiodinated MEC were solubilized and subjected to affinity chromatography on Fn-Sepharose columns, two polypeptides of 150 and 125 kD, corresponding to the integrin heterodimer .alpha.5.beta.1, were identified. MEC also express a complex of 150 (.alpha.) and 95 kD (.beta.3) that is related to the Vn receptor. Immunofluorescent staining of MEC cultures with antibodies to the integrin .beta.1 subunit demonstrated receptors on the basolateral surface a focal adhesion plaques that co-localized with vinculin and with Fn-positive matrix fibers. Occasionally, antibodies to the Vn receptor stained the vinculin-positive focal adhesion plaques that frequently co-localized with the .beta.1 complex. However, in cultures of MEC that were attached to substrates coated with alternating strips of Fn and Vn, the .beta.1 complex was preferentially localized to the Fn substrate, while the Vn receptor was concentrated on the Vn substrate. The results indicate that MEC express at least two different heterodimer adhesion receptors that belong to the integrin superfamily and appear to have distinct ligand specificities: the Fn receptor and the Vn receptor. These receptors mediate cell adhesion to the extracellular matrix and presumably have an important role in hemostatis and neovascularization.

12/7/42
DIALOG(R)File 5:Biosis Previews(R)

09697878 BIOSIS NO.: 198988012993
ADHESION OF LYMPHOID CELLS TO THE CARBOXYL-TERMINAL HEPARIN-BINDING DOMAINS OF FIBRONECTIN
AUTHOR: LIAO N-S (Reprint); ST JOHN J; MCCARTHY J B; FURCHT L T; CHEUNG H T

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JOURNAL: Experimental Cell Research 181 (2): p348-361 1989
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Previously, we have shown that some lymphoid cell lines adhere to fibronectin (FN)-coated substratum, whereas others do not. In this study, the adhesion of five adherent lymphoid cell lines to different FN domains was examined. These cell lines ranged in their adherence to substratum coated with FN, the cell-binding domain (CBD) fragment, or the heparin-binding domain (HBD) fragments. None of the cell lines adhered to substratum coated with the %%%gelatin%%%-binding domain fragment. Three of the lymphoid cell lines adhered preferentially to HBD over CBD, whereas two other lymphoid cell lines and BHK fibroblastrs adhered preferentially to CBD. These results suggest that two distinct adhesive interactions occur between cells and FN and that the pattern of interaction varies among cell types. Using MOPC 315 (which adheres preferentially to HBD) as a cell model to study the cell-HBD interaction, the HBD-promoted adhesion was found to be independent of the %%%RGD%%% sequence and could be inhibited by anti-FN antibodies. Moreover, the MOPC 315-HBD interaction had the following characteristics: (1) adhesion was temperature dependent, (2) presence of divalent cations was necessary, (3) integrity of cellular microfilaments but not microtubules was required, (4) inhibition of protein synthesis abolished adhesion, (5) pretreatment of cells with trypsin inhibited adhesion, and (6) the adhesion was mediated by the carboxyl-terminal HBD.

12/7/43
DIALOG(R)File 5:Biosis Previews(R)

09570018 BIOSIS NO.: 198987017909
A COLLAGEN-BINDING PROTEIN INVOLVED IN THE DIFFERENTIATION OF MYOBLASTS RECOGNIZES THE ARG-GLY-ASP SEQUENCE
AUTHOR: NANDAN D (Reprint); CATES G A; BALL E H; SANWAL B D
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JOURNAL: Experimental Cell Research 179 (1): p289-297 1988
ISSN: 0014-4827
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We had earlier demonstrated that a 46-kDa glycoprotein is involved in the differentiation of rat skeletal myoblasts. We now show that the binding of this glycoprotein to collagen and %%%gelatin%%% is disrupted by Arg-Gly-Asp (%%%RGD%%%) containing peptide but not by Arg-Gly-Glu (RGE). The former peptide also selectively elutes the 46-kDa glycoprotein bound to %%%gelatin%%%-Sepharose. Since all other proteins which bind %%%RGD%%% sequences have been found at the cell surface, we attempted to localize the 46-kDa glycoprotein by means of immunofluorescent staining and radioiodine labeling. Surprisingly, the majority of the protein was found to be localized in the endoplasmic reticulum. Protease treatment of a microsomal fraction revealed that the

protein is in the interior of the reticulum. Immunoprecipitation experiments, using a polyclonal antibody against the 46-kDa protein, demonstrated that no closely related proteins exist in myoblasts and also confirmed that the protein was not a fragment of a cell-surface localized protein. These findings suggest that the %%%RGD%%% sequence is also used in protein recognition within the cell.

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Set     Items   Description
S1        537   RGD AND COLLAGEN
S2          3   RGD(2W)ENRICH?
S3         20   S1 AND GELATIN?
S4          2   (RGD(2W)IN()COLLAGEN)
S5         59   GELATIN? AND RGD
S6         16   S5 AND INCREASE?
S7          0   (ADD(3W)RGD()COLLAGEN)
S8          0   INSERT()RGD
S9          4   INSERT?()RGD
S10         0   INSERT AND RGD AND COLLAGEN
S11         0   INSERT AND RGD AND GELATIN?
S12        43   S5 NOT S6
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   $250.64  Estimated cost File5
     $5.33  TELNET
   $255.97  Estimated cost this search
   $255.99  Estimated total session cost   6.186 DialUnits
Logoff: level 05.21.01 D  14:31:43
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